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ROYAL COMMISSION OF INQUIRY INTO CERTAIN DEATHS AT THE HOSPITAL FOR SICK CHILDREN AND RELATED MATTERS.

Hearing held 8th floor 180 Dundas Street West Toronto, Ontario

The Honourable Mr. Justice S.G.M. Grange

P.S.A. Lamek, Q.C.

E.A. Cronk

Thomas Millar

Commissioner

Counsel

Associate Counsel

Administrator

Transcript of evidence for October 18, 1983

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1 ROYAL COMMISSION OF INQUIRY INTO CERTAIN DEATHS AT THE HOSPITAL FOR SICK CHILDREN 2 AND RELATED MATTERS. 3 4 Hearing held on the 8th Floor, 5 180 Dundas Street West, Toronto, Ontario, on Tuesday, the 18th 6 day of October, 1983. 7 8 THE HONOURABLE MR. JUSTICE S.G.M. GRANGE - Commissioner 9 THOMAS MILLAR - Administrator 10 MURRAY R. ELLIOT - Registrar 11 APPEARANCES: 12 Commission Counsel P.S.A. LAMEK, Q.C.) 13 E. CRONK D. HUNT Counsel for the Attorney-14 L. CECCETTO) General and Solicitor General of Ontario (Crown Attorneys 15 and Coroner's Office) I.J. ROLAND) 16 Counsel for The Hospital for M. THOMSON) Sick Children R. BATTY 17 S. GRANT Counsel for The Metropolitan 18 D. YOUNG Toronto Police 19 Counsel for numerous Doctors K. CHOWN at The Hospital for Sick 20 Children Counsel for the Registered 21 F. KITELY Nurses' Association of Ontario and 35 Registered Nurses at 22 The Hospital for Sick Children 23 (Cont'd)

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1	APPEARANCES:	(Continued)
2	D. BROWN	Counsel for Susan Nelles - Nurse
4	G.R. STRATHY) E. FORSTER) P. DODDS)	Counsel for Phyllis Trayer -
5	J.A. OLAH) A. ARNOLD)	Counsel for Janet Brownless - R.N.A.
7	B. JACKMAN	Counsel for Mrs. M. Christie - R.N.A.
8	S. LABOW	Counsel for Mr. & Mrs. Gosselin, Mr. & Mrs. Gionas, Mr. & Mrs. Inwood, Mr. & Mrs. Turner, and
9		Mr. & Mrs. Lutes (parents of deceased children)
11 12	F.J. SHANAHAN	Counsel for Mr. & Mrs. Dominic Lombardo (parents of deceased child Stephanie Lombardo); and Heather Dawson (mother of deceased child Amber Dawson)
13 14	W.W. TOBIAS	Counsel for Mr. & Mrs. Hines (parents of deceased child Jordan Hines)
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NAME Page No. SOLDIN, (Dr.) Steven John, Resumed Cross-Examination by Mr. Strathy (Cont'd) Cross-Examination by Mr. Hunt Cross-Examination by Mr. Young Cross-Examination by Ms. Jackman Cross-Examination by Mr. Olah Cross-Examination by Mr. Roland Re-Direct Examination by Ms. Cronk



/DM/ak

---Upon commencing at 10:00 a.m.

THE COMMISSIONER: Before you may start, Mr. Strathy, I have dictated something rambling about the evidentiary problems and I am going to read it. Mr. Lamek has copies of it and of course it will appear in the transcript.

Mr. Sopinka has raised two questions.

- (1) That no question should be put in evidence intended to elicit an answer indicating who committed an alleged crime, and
- (2) That the Police Report, that is the report of the Metropolitan Toronto Police referred to by the Attorney General in his report to the legislature, should be produced to him and presumably to other Counsel concerned.

As to (1), Mr. Sopinka concedes, as I understand it, that such evidence may be relevant for another purpose, namely to determine the cause of death. He asks, however, that before it is received some effort be made to explore how it can be done without implicating an individual.

I am sympathetic to his position and, particularly, am concerned about the unfairness it may cause a party if the evidence is adduced at a

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time when the opportunity to answer is to be long delayed. Nevertheless, I cannot make a blanket ruling for several reasons as follows:

- (a) I cannot know in advance of the evidence being tendered whether the evidence will be relevant to Phase I. Each instance must be considered at the time it is tendered.
- (b) The problem is not yet resolved as to whether the Terms of Reference which require me to report on the cause of death permit me to express any opinion as to the complicity of any person in the deaths. As will be seen, I am suggesting that there be argument upon that question.
- (c) It is abundantly clear to me that the apparent complicity of Susan Nelles, at least up till the time of her release after the Preliminary Inquiry, is relevant to the determination of the issues in Phase II.

To prevent an injustice, not in the Commission but in the reporting of the proceedings in the media, I will certainly entertain any motion for immediate cross-examination or for evidence out



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of turn or for any other relief whenever a party's complicity is implied. I hope that will not be necessary but an example has already been demonstrated during the evidence of Dr. Fowler.

The second issue relating to the Police Report clearly is arguable. As the Counsel most concerned are Mr. Sopinka and Mr. Percival, I suggest that they agree upon some time, preferably at 3:45 in the afternoon and the argument can then take place. Of course it is open to Counsel to resolve the matter without argument.

There are two further matters which are not so urgent but I am satisfied must be resolved in the interests of a fair hearing. They are first the issue referred to above, namely whether I can in the Report if I should find that there was a deliberate overdose of Digoxin contributing to the deaths of any baby implicate any person in that overdose, or to put it in Mr. Scott's words, If I can "name names". Secondly, some Counsel have suggested that evidence in Phase II should not include anything that occurred after the release of Susan Nelles at the Preliminary Inquiry. I think the problems lend themselves to written argument and I would ask any Counsel having an opinion on either matter to submit that written argument to me by November 1st, 1983. That argument will be distributed among all Counsel on that day and each Counsel will have an opportunity to reply by



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November 10th. I remind all Counsel that the essential question is what the Terms of Reference permit or require.

There is just one other matter I wish to raise at this time. Mr. Sopinka suggests that no finding of misconduct can be made against any person unless a formal notice of misconduct is given and presumably all the evidence given thereafter. I do not so interpret the section which calls only for reasonable notice of the substance of the misconduct alleged against him and full opportunity to be heard in person or by Counsel. I cannot imagine that there could ever have been the slightest doubt as to why each member of the Trayner team is here represented by Counsel funded by the Province. If such a doubt has ever existed, let me make it now quite clear that each of them may be found to be implicated either by accident or with deliberation in the deaths of the children. I emphasize that to date very little of such evidence has been presented but it is anticipated that some evidence will be tendered and of course Counsel for the parties concerned will be entitled during the hearing to be heard and to adduce evidence relevant to the issues before this Commission.

I suggest, ladies and gentlemen, it is



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probably wise to read the matter over before you make any comments on it. I will entertain comments any time anyone wants, but failing that the two matters are for Mr. Percival and Mr. Sopinka to make arrangements for the time for arguing; and the other one is anyone who has any comments on the two questions I raised to submit written argument by the 1st of November.

Yes, Mr. Strathy?

MR. STRATHY: Just before I resume my cross-examination, Mr.Commissioner. I understand what you have said about not making any submissions on your comments until we have had an opportunity to reflect on it.

THE COMMISSIONER: Yes.

MR. STRATHY: I would like to make

submissions.

THE COMMISSIONER: Yes, all right.

MR. STRATHY: But not necessarily at

this stage.

THE COMMISSIONER: No, fine.

MR. STRATHY: I had understood when Mr. Sopinka made his submissions the last day it was simply a proposal to you which he wanted to argue at a later date.





THE COMMISSIONER: Yes.

MR. STRATHY: And I withheld my comments at that time because I understood there would be an argument at a later date and I think Mr. Sopinka refrained from making his full pitch to you for the same reason.

it it was whether it was worthwhile taking the time even to argue the matter. I have now indicated that I am not prepared to give a ruling with respect to that, but each time it comes up the question can be raised, there is no problem it can be raised if it comes up, but it hasn't come up since. I am not going to hear argument on that question now because in my view it would be impossible to deal with it.

MR. STRATHY: Well I think,

Mr. Commissioner, there may be a need for argument on other questions, including the question of notice and including the question of your Terms of

Reference.

THE COMMISSIONER: Well, that is what

I am suggesting there be written argument on that.

I suggest there be oral argument on the police report,

and I am suggesting that if you want to put it that

my mind is closed to the matter there is no point in



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having argument on the first question.

MR. STRATHY: The first question being?
THE COMMISSIONER: The first question
question as to whether or not, as I put

"That no question should be put in evidence intended to elicit an answer indicating who committed an alleged crime,..."

And I have said that I am sympathetic to the position and I declined to make a blanket order.

MR. STRATHY: I wonder if you might extend your area of written submissions to the question of notice. Because I would support Mr. Sopinka's position on this issue, and that there has to be specific notice and the blanket notice is not ---

suppose we could have that. What I really was doing was that you can raise that as a motion at any time you like and you can certainly submit written argument on it if you want to. I am telling you now that I do not intend to have this Commission go through the evidence all over again as Mr. Sopinka was suggesting, that is if we have to give notice at some time of some particular complicity and then go through all the





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evidence again, I don't intend to do that.

MR. STRATHY: I think Mr. Sopinka would have wanted to have an opportunity to present argument to you on that very point.

THE COMMISSIONER: Well, I thought he did, and I told him I didn't accept that.

MR. STRATHY: It was my impression that he started to refer to some of the authorities.

appear at any time and put his position and you can put your position at any time. I have indicated a pretty firm view on the matter to you. Your client, Mr. Sopinka's clients, and several other clients have been I think on notice since the beginning of this Hearing on what the problem is that they are facing. If I haven't made it clear in this I don't see how I could possibly make it clearer. So reasonable notice, it doesn't say written notice, it says reasonable notice of what misconduct might be found against them and an opportunity to reply to it.

MR. STRATHY: I might say with respect I don't agree that is notice within the meaning of the Statute and I think that is the position Mr. Sopinka is taking.

THE COMMISSIONER: Well ---





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MR. STRATHY: But I understand what you have said.

THE COMMISSIONER: Yes.

MR. STRATHY: The only other point I want to raise, Mr. Commissioner ---

THE COMMISSIONER: I may out of an abundance of caution give another notice, I don't say I won't, but I may after, but that notice will not be a notice intending to permit the whole to proceed again. If that is what the legislators meant they need their heads bent, because you can't run a Commission that way.

MR. STRATHY: I may get into the issue as to what the legislators meant in the Statute.

THE COMMISSIONER: Yes.

MR. STRATHY: The only other point, sir, Mr. Sopinka asked for the Police Report. Now as I understand it the Police Report is something that-the brief that the police prepared to assist the Crown Attorneys ---

THE COMMISSIONER: No.

MR. STRATHY: --- and that Mr. Sopinka or his predecessor ...

THE COMMISSIONER: I have seen that.



No, I think the Police Report that we are talking about is the Police Report that the Attorney General read, that the Attorney General made reference to in his statement, isn't that the one we are referring to?

MR. YOUNG: That is correct,

Mr. Commissioner.

THE COMMISSIONER: That is the one you have in mind is it not?

MR. YOUNG: It is the report that was prepared for the Chief of Police.

THE COMMISSIONER: Yes.

MR. STRATHY: May I ask when it was

prepared?

THE COMMISSIONER: It was prepared at any rate before the Attorney General made his statement which would have been at the end of April of this year. Do you know the date of it?

MR. LAMEK: It is dated February, 1983

THE COMMISSIONER: February of 1983,
that is the Police Report upon which the Attorney

General acted.

MR. STRATHY: All I say is this. Until we have seen the document we really don't know what it does and does not include and there may be other things that would be required to be argued.



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THE COMMISSIONER: But that is all he asked for, if you want to ask for something else afterwards you can always ask for that.

MR. STRATHY: I just wanted to make that clear.

THE COMMISSIONER: Yes. You probably have discovered by now that almost, practically none of my rulings are carved in stone but I thought it would be a good idea to tell you about these so that you would understand what was happening. If someone wants to ask a question that they imply some complicity of some particular person, some crime, it has to be objected to at that time either as to relevance or as to some other relief that is wanted, because that is the way I am going to act.

As far as the Police Report is concerned it will not be released to anybody until the argument has been heard and I have made a ruling. As far as the other two matters are concerned they obviously will not be decided until after November the 10th when all the argument is in. So far as the notice question is concerned I have made my statement and. I may decide with an abundance of caution I will give another notice to certain persons and I may not.

MR. STRATHY: Thank you.

THE COMMISSIONER: All right.



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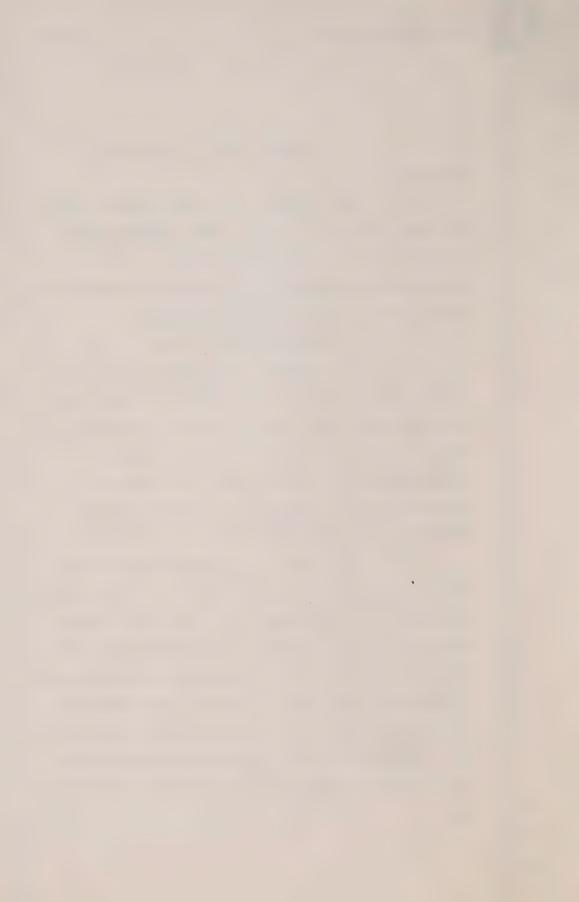
All right. Now, do you want to

MR. ROLAND: Mr. Commissioner, before my friend proceeds. I wasn't here yesterday but I gathered at the end of the day there was some excitement as a result of Dr. Soldin's disclosure of ongoing experiments that he was having.

THE COMMISSIONER: Yes.

MR. ROLAND: And just to make it clear to all the participants and to you, Mr. Commissioner, Miss Cronk and I met with Dr. Soldin a week ago last Friday in which she interviewed him to prepare her examination of Dr. Soldin, which was done by her yesterday and, in the course of that, there was mention of these experiments that were ongoing.

Dr. Soldin indicated to Miss Cronk
and to me that he would prefer not to get into those
experiments at this stage because they were ongoing
and that he hadn't arrived at any conclusions from
them at that stage or any definitive conclusions and
I understand since then of course he has made some
additional discoveries. Experiments are moving along
at a rapid pace now but they are still ongoing and
Dr. Soldin is reluctant to get into the details of
them.





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He has given you, I understand, yesterday, I have reviewed the transcript, a summary of what he has been doing and some of his earlier and tentative conclusions but the experiments continue and are continuing throughout this week. He indicates to me that the next two or three weeks may be very exciting weeks for him in terms of this experiment.

I want it to be made clear in fairness to Commission counsel and I think to the Hospital that we intended, I think Commission counsel intended and certainly the Hospital intended to put all of that material before you when the experiments reached a more definitive conclusion than they have to date.

THE COMMISSIONER: Yes. Well, I can well understand your reason for saying this but there is not much we can do about it now.

MR. ROLAND: No, there isn't.

THE COMMISSIONER: Mr. Strathy has

raised the issue.

MR. ROLAND: Yes, he has.

THE COMMISSIONER: And if he wants to pursue it I can't tell him he can't.

MR. ROLAND: No, that's true. That's true. I have no objection to Mr. Strathy pursuing it but I didn't want the sense to be left that anybody





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was hold:--

was holding back on this material in this Commission, Commission counsel or the Hospital, but that we understood from Dr. Soldin, at least ten or twelve days ago, that he would prefer to leave his evidence on this series of experiments until he had reached a more definitive conclusion.

THE COMMISSIONER: Unless somebody will guarantee that he will come back, and I hope nobody will guarantee me that because there is nothing I like better - I guess the only thing I like better in seeing a witness come up to the stand is to see him leave in the hope that he will never come back at all, so, I don't know.

MR. ROLAND: With great respect,
Mr. Commissioner, I would have thought you would be
very anxious to know when a series of experiments
are concluded, what the results are.

THE COMMISSIONER: Well, there is no question that I would like to have that. If he has nothing to say, if it develops that he does his experiments and he can give us no more I don't want to see him.

MR. ROLAND: I understand that. If the experiments turn out to be faulty in some way in which he has conducted them or inconclusive and so on,





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and can't assist the work of this Commission, then obviously he wouldn't come back. He is in the course of conducting those experiments now. He has some early and tentative conclusions and he has given those to Mr. Strathy yesterday I understand.

I quite agree, Mr. Strathy can continue to pursue that line if he so chooses today. What I want to indicate to you is that those will continue, those experiments will continue and be ongoing and if they arrive at some conclusions that may assist this Commission's work, then we or the Commission counsel I presume will call him back so that he can give you the benefit of those conclusions.

MR. HUNT: If I could just make a comment, Mr. Commissioner.

THE COMMISSIONER: Yes.

MR. HUNT: I don't know if you intend to restrict any of the cross-examination but I appreciate my friend wasn't here yesterday for the dramatic announcements by the witness himself at the end of the day but I didn't get the impression from anything the witness said that we were into a research situation or an experimental situation here.

He indicated to us at page 1368 that he had developed an assay for the measurement of





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digoxin by liquid chromatography as well as mass spectrometry and definitively, and that was his word, not anyone else's.

THE COMMISSIONER: Yes, isolated to Substance X.

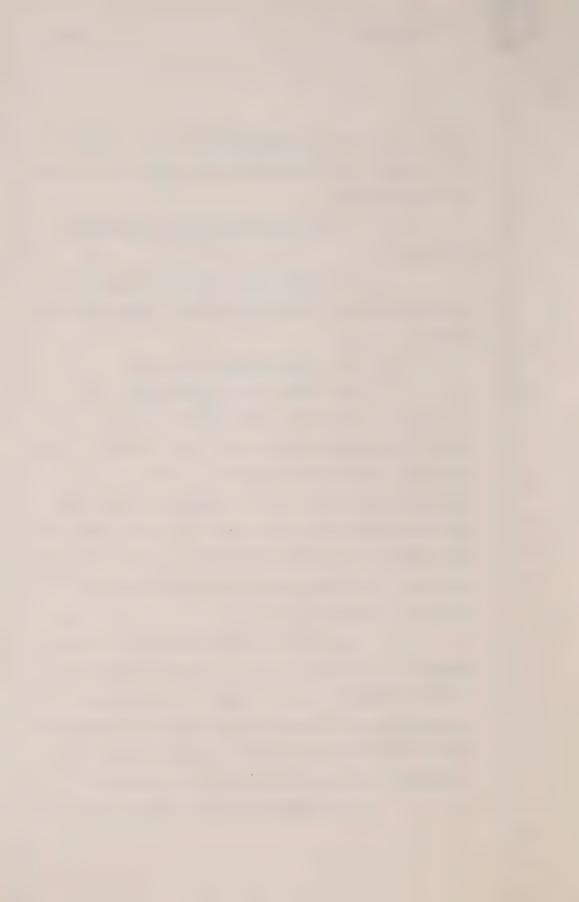
MR. HUNT: So that this compound is digoxin and cannot be anything else. Those were his words.

THE COMMISSIONER: Oh, yes.

MR. HUNT: The witness then went on to ask for samples back from either the police or the Centre of Forensic Sciences and, quite frankly, I was certainly under the impression as of the end of yesterday that this was not a research project that the witness was asking us to participate in with him but before he would make comments like that he was to the point in his work where he could make some scientific statement about it.

Now, that having been opened by the witness, I think there may be a need to explore that with him before he leaves today. I appreciate my friend may not have been aware of quite precisely the import of the witness' comments yesterday, but that certainly is my understanding of the situation.

MR. ROLAND: I don't quarrel with what





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Mr. Hunt has to say. I think there are two issues here: one is the analysis of some tissue to determine if indeed digoxin is or is not in those particular tissues being analyzed and, as I understand it, and having looked at the transcript yesterday and spoken to Dr. Soldin, that he is able to do that. That is now what I was talking about. I was talking about the issue of an endogenous substance, Substance X or Y or Z or whatever it is in all of us, and the circumstances in which it may find its way into body serum or urine and so on. That is a different issue and that is the experimental part of his studies.

THE COMMISSIONER: Yes, all right.
Miss Cronk?

MS. CRONK: Yes, Mr. Commissioner. If it assists you, I share a certain of Mr. Hunt's submissions to you. It was certainly my understanding on the basis of the evidence that the witness gave yesterday that he had put forward the nature of the studies that were being conducted and the results at a level that I had not understood was yet prepared to advance the matter and because of the way the evidence went in on that aspect yesterday it is certainly my intention to explore the issue with the witness further in re-examination if my friends do not,





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particularly in light of what I understood him to say at our pre-evidence meeting that Mr. Roland has referred to.

THE COMMISSIONER: Yes. Well, I am not going to restrict anybody's cross-examination and I don't think we can count on the return of Dr. Soldin. It may well be that he will return with all sorts of interesting information but I think you have to act upon the assumption that he will not.

All right, Mr. Strathy.

MR. STRATHY: Well, I just would like to put my two cents in before I start to cross-examine.

I would say to you, Mr. Commissioner, that I have a concern that this sort of evidence that we have gone into yesterday in my cross-examination has to come out through me and it doesn't come out through Commission counsel.

THE COMMISSIONER: That's what Mr.

Roland and ---

MS. CRONK: Now, just a minute.

MR. STRATHY: I would like to finish

my submission.

THE COMMISSIONER: Yes, all right.

MR. STRATHY: It is very interesting

that research is going on and I am sure it is





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fascinating to the Hospital and the university and to the witness but obviously this is a public exercise and it is important that the evidence be presented when it is available and it concerns me that Commission counsel have knowledge of this sort of research going on and that it is not brought out.

Now, they are the people that have control over the evidence and in normal circumstances one might well say, well, all right, we won't deal with it because it is a research project but surely in a public inquiry it is important that this be brought out.

the matter was put before you that the witness himself said, this is what I understood from Mr. Roland, the witness himself said that he was not yet in a position to give any evidence and would prefer not to and for that reason it wasn't pressed. And then he volunteered, almost volunteered when you were cross-examining, so, clearly he had either thought better of it, changed his mind or something but he had something that he wanted to say.

I don't know really, I don't see any fault on the part of anybody. If the witness says I am doing some work on something, I am not in a





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position to give any evidence on it, I would prefer not to do it, it is not unreasonable not to press him.

MR. STRATHY: Well, that might be so in other circumstances but surely the very fact that he is doing the research is relevant to the Commission. Surely the fact that the Hospital thinks there may be an explanation for all this may be relevant.

MS. CRONK: Mr. Commissioner, I must rise to this. Whether or not my friend intended, I take great offence at the suggestion that has been made. As Mr. Roland suggested, and I will take it one step further, it was my very clear understanding on the basis of the meeting that I held with Dr. Soldin before he came back to testify that not only was he not in a position to testify with respect to these results but he himself was not prepared to attest at this stage as to the validity and were he subsequently in a position to do so we would then have adduced that evidence.

THE COMMISSIONER: Yes, all right.

MS. CRONK: And I made that specifically

clear to Mr. Strathy yesterday afternoon.

Now. Mr. Roland, you want to make a statement?

THE COMMISSIONER: Yes, all right.

MR. ROLAND: Yes. I think I was at





that meeting as well and I am not as hot about it as Miss Cronk is ---

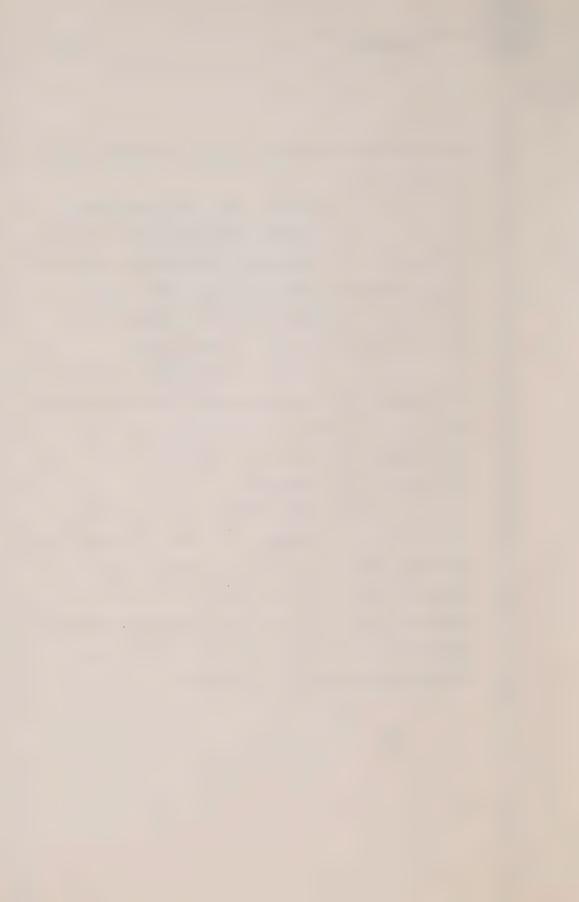
MS. CRONK: And I'm getting hotter.

MR. ROLAND: Basically what she said is accurate that the witness indicated to us that he wasn't prepared at this stage or at that stage to talk about it because it was still ongoing and he would prefer to leave it to a later stage.

To be fair to the witness as well it is ongoing and the experiment is at the last ten days and indeed this week are at critical points and information is coming in at a great pace. It is at that stage of the experiment.

THE COMMISSIONER: Yes, all right.

MR. ROLAND: So, when the witness said to us ten days ago he wasn't prepared to testify on the information he had then, to be fair to the witness I think he has had some additional information since then and he will continue to acquire more information over the next few weeks.





18oct83 C EMTra THE COMMISSIONER: All right. Now I think we have had all the statements we want to have.

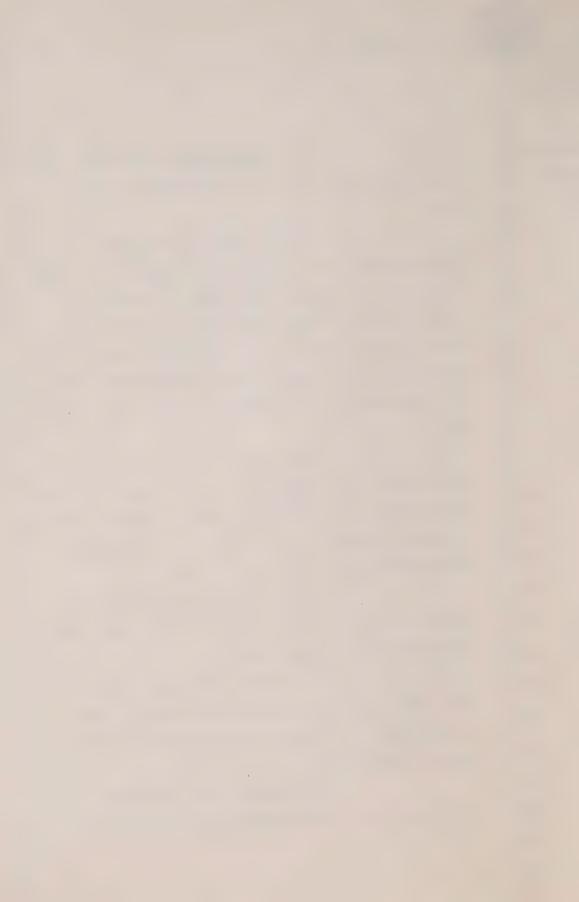
Do you want to get on with the cross-examination? You are not limited in any way, and I would like you to put most of the rest of your comments to the witness, but if you have one more thing you want to say, please don't say it in a way that will require or will automatically knee jerk reaction from Mr. Roland or Miss Cronk, that is all.

MR. STRATHY: Well, Mr. Roland is a very honourable gentleman and Miss Cronk is a very honourable lady, and I don't want to suggest there is anything improper in what they did. That should leave them seated for a little while.

But it does seem to me that we should have Dr. Soldin back at some time after this research has been completed.

THE COMMISSIONER: Well, we will see about that, and you can always apply, if he doesn't turn up at somebody's auspices, you can apply for a subpoena.

MR. STRATHY: Mr. Roland has indicated to me that the Hospital will call the



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doctor if there is anything further that comes to light in the course of his research.

May I ask that the doctor resume the stand then?

THE COMMISSIONER: Yes. All right.

Thank you.

STEVEN JOHN SOLDIN, Resumed

THE COMMISSIONER: Yes, Mr. Strathy.

CROSS-EXAMINATION BY MR. STRATHY (Continued):

Q. Doctor, towards the end of the day yesterday you made a request that samples be produced for you so that you could perform an analysis, and I want to be sure, please, what that analysis was that you intended to do.

Now can you assist us, please, as to what methodology you intended to apply?

A. Well, I would like to add a cautious note first of all: The analysis that we would attempt to apply to materials, were they available, would involve high performance liquid chromatography, extensive high performance liquid chromatographic separations; not just a single analysis by HPLC, and would involve mass spectometry of column eluents which are found to have digoxin activity.



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Mass spectometry or gas

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HPLC to separate the elements and then apply gas spectometry -- mass spectometry. A.

chromatography, mass spectometry, yes. Either MS or GCMS to the purefied preparation that has digoxinlike activity.

O. So it would be a combination of the two processes then?

> Correct. A.

0. That would enable you to determine whether the substance is digoxin or something other than digoxin?

A. Hopefully that would be the case, yes. Now what the actual concentrations of let us say digoxin or Substance X are in either the tissues or the body fluids that might be provided may or may not enable this study to be performed with an appropriate conclusion being reached.

All right. That is 0. something we will have to find out in due course obviously.

> Yes. A.

Doctor, are you familiar Q.



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with the methodology adopted by Mr. Cimbura in his analysis of various tissue samples from the bodies of some of the children we are dealing with?

A. Well, I was here for his evidence. Now that doesn't mean that I am familiar with all his techniques.

Q. Well, let me put it to you -- sorry. My understanding is that he used a combination of high pressure liquid chromatography and radioimmunoassay. Is that your understanding?

A. Yes.

Q. And as I gather what you are suggesting is that you would go considerably further than that?

A. Well --

Q. Because you would have

mass spectometry?

A. I would add mass spectometry, yes, and we would do extensive high performance liquid chromatographic runs.

Q. More than just the one

Mr. Cimbura did?

A. I don't know how many he did. I can tell you we do many.

Q. When you say "many", how



Five or so.

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many are you talking about?

Α.

Q. On the basis of your understanding of Mr. Cimbura's methodology do you have concerns as to whether or not you would be able to isolate the digoxin from other substances using his methodology?

A. If you are asking whether I have concerns whether he can separate digoxin from Substance X using HPLC and radioimmunoassay, yes, I have some concerns about that.

Q. And is that why you are not only doing several HPLC runs but also applying mass spectometry?

A. Yes, that is correct.

Q. Is it fair to say that your methodology is a more refined methodology?

A. Well, mass spectometry as I said yesterday is a definitive procedure. It identified compounds. So it would be able to identify digoxin. It would be able to identify Substance X. It would be able to distinguish between the two.

Q. And it is your view that if you are able to apply these tests to specific

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samples or some of the specific samples taken from the bodies of children who died during this period, you will be able to tell whether the readings are readings of digoxin or readings of something else?

A. Provided sufficient material is given to our group I think that may be possible, yes. May be possible, and I am cautious about it.

 $\label{thm:concentrations} \mbox{It depends on the actual concentrations of either digoxin or Substance X in these $$ $$ \mbox{materials.}$

If we get sufficient material, one should be able to definitively establish whether or not it is digoxin or Substance X.

 Ω_{\bullet} Do you know from what you found out between last night and this morning whether that material is available or not?

A. No, I have no idea.

MR. YOUNG: If my friend wishes me to interrupt him, I have made some enquiries of officers, Mr. Commissioner, and if there are any samples, they would be with the Centre for Forensic Sciences. They are not with the police. We do not have any.

MR. HUNT: Yes, an inventory is



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being made today of what samples are still at the Centre and what condition they would be kept in, what solution --

THE COMMISSIONER: What happened to the exhibits at the preliminary inquiry? Were any of these made exhibits?

MR. HUNT: I may stand corrected, but anything that had to be kept in a preservative or refrigerated is at the Centre as I understand.

MR. YOUNG: I am informed, Mr. Commissioner, that no actual samples were made

exhibits at the preliminary.

THE COMMISSIONER: Well, presumably then they still would be with the Centre if they are there.

MR. HUNT: Oh, there is material

THE COMMISSIONER: Yes.

MR. HUNT: As I say, I can't tell you what it is because I am told it will take a day to inventory it all and that will be done today.

THE COMMISSIONER: Yes.

MR. HUNT: So the information

should be available tomorrow.



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THE COMMISSIONER: Yes. All right.

MR. STRATHY: Q. Doctor, turning to another subject you mentioned in your evidence yesterday you had in your experience found levels of in excess of 50 nanograms per millilitre of digoxin in I think it was serum where contamination had occurred. Contamination I take it of the sample.

Do you recall your evidence in

Q. I have it in my notes.

A. We found high digoxin concentrations in certain samples that had been contaminated. I don't know if I mentioned greater than 50. Maybe you could refer me to the page there?

I don't have the page reference, doctor, but that was my recollection that you mentioned the figure of greater than 50 in your examination by Miss Cronk.

A. Well, we have had high

value --

that regard?

MR. LAMEK: At page 1313.

MR. STRATHY: I beg your pardon?

MR. LAMEK: Page 1313, sir, line 3.





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MR. STRATHY: Thank you. Yes, thank you, Mr. Lamek.

0. You mentioned in the context, Doctor, of referring to different ways that you could get elevated levels, and you mentioned one is the possibility of timing as the sample being taken fairly soon after administration. Then you said:

> "We have had experience of concentrations over 50 when there was contamination of the sample.

We have had concentrations over 50 when there was contamination of the sample."

My first question is when were those experiences of contamination?

A. They have happened at various times since I took over the digoxin procedure.

This is in the context of therapeutic monitoring program?

A. Correct, yes.

And my recollection that was 0.

July of 1981?

Something like that, yes. Α.

Now we have had high concentrations, I am not happy with saying that they definitively are over 50 in



number. We have had some high concentrations, some-



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where between I think 20 and 50.

Q. All right. My next question is how have those contaminations occurred?

A. Well, I guess there are several routes and possibilities. One would be if digoxin was given in a syringe, and then that same syringe is used to draw a blood sample, that syringe would have a lot of digoxin still sticking to the walls of the syringe and you get a very high measurement.

Another is if digoxin is given in a particular site with an ingraining line, we have an ingraining line in a lot of these patients, digoxin might be administered and then the serum sample, or a blood sample could be drawn shortly thereafter for measurement of a number of things, including digoxin and you could get contamination from that factor.

Obviously whenever we obtained a very high result of this type it was immediately repeated on a stat basis on that patient. It is not a frequent occurrence but it has happened maybe three times since July of 1981.

Q. All those being circumstances though of contamination in living patients?





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Α. Yes, the patients have never shown any clinical signs of digoxin toxicity.

Q. And the patients were all alive at the time the samples were taken?

They were all alive medically, A. yes, to my knowledge.

Q. Doctor, you mentioned that, I believe it was in connection with the Miller child, that you requested a specimen of the digoxin elixir so you could submit it to analysis?

> A. Yes.

Was that request from you? Q.

Yes, I think, I believe it A.

To whom? Q.

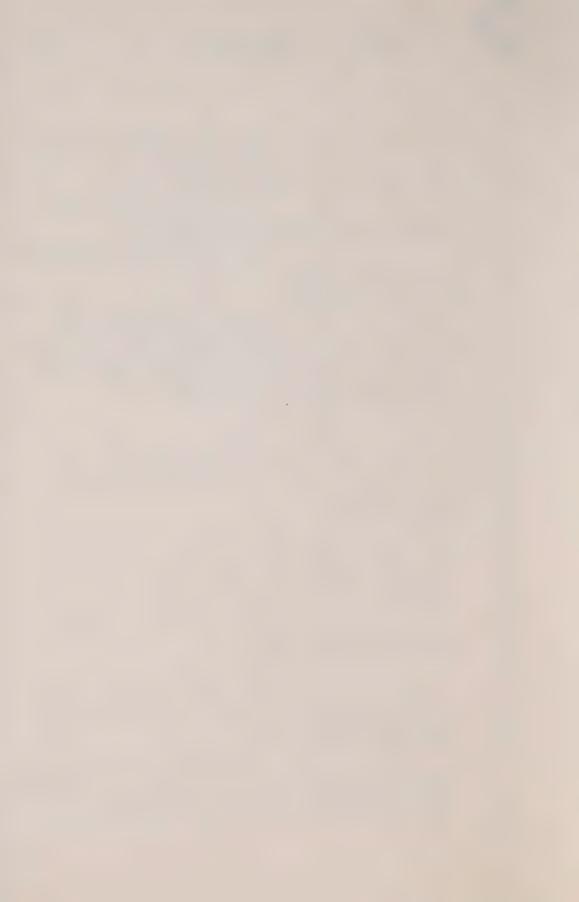
To the doctors that were on A. that ward, I think it was Dr. Costigan.

And when you say on that 0. ward, do you mean 4A/4B?

> 4A/B, yes. Α.

And did you yourself see the specimen that was obtained?

Subsequently, yes, it came in after the analysis had been carried out and subsequently I saw whatever preparation had been obtained.





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2	Q. Was it your understanding it
3	was digoxin paediatric elixir?
4	A. Yes.
5	Q. Do you know, was it a full
	bottle?
6	A. I can't recall how full, but
7	I think it was fairly full.
8	Q. Do you know how much was take
9	out of the bottle in order to test it?
10	A. To do the dilution?
11	Q. Yes.
12	A. I must have directed the
	technologist, I can't recall if I told her to dilute
13	one ml 10,000 times, or if I told her to dilute 100
14	microlitres 10,000 times, I would have given her the
15	guidelines.
16	Q. Is it only one bottle to your
17	recollection?
18	A. Yes, at that time it was only
19	one. I am not sure if I mentioned yesterday we did
	measure another bottle some time before that, did I
20	mention that?
21	Q. I am sorry.
22	A. On the Wednesday before Allan
23	Miller passed away, or on the Thursday, we measured





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another preparation of digoxin from that ward.

Q. And what were the circumstances of measuring that sample?

recall it this was the first knowledge that I think I had of any possible problem with digoxin in the hospital, and Dr. Hill had a meeting with - he called me into his office and said there was some problems with digoxin, possibly with the medication and that he thought we should check out some of the medication on Ward 4A/4B which is what - I then went and got a bottle of it and gave it to Dr. Ellis who was running the dig. assays at that time and he measured digoxin in that particular sample and I think that was on the Thursday that the measurements were made.

Q. Do you recall where you got that bottle from on the Thursday?

- A. From Ward 4A/B, yes.
- Q. Was it a full bottle?
 - . It was I think a pretty full

bottle, yes.

- Q. Really my question is was it a bottle that had been in use, or was it a fresh bottle from the shelf?
 - A. I don't believe it was a fresh



Soldin, cr.ex. (Strathy)

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bottle, it was a bottle that had been in use.

- Q. But your recollection is it was relatively full?
 - A. Correct.
 - Q. Just one last area, Doctor.

There have been some statements this morning - we opened making comments about your research, and perhaps we should find out from you what exactly it is that is going to be taking place in these exciting weeks to come. What is it that you have in mind to do?

I guess one of the things you are going to do if you can get these samples from Mr. Cimbura's refrigerator is to apply your test to the samples?

A. Well, that would be one of them, yes.

Q . I don't want you to give away any secrets for your publications, but can you give us for the assistance of the Commission some indication where you are going?

THE COMMISSIONER: I am far more interested in this Commission rather than in his publication.

MR. STRATHY: That is what I say.

THE COMMISSIONER: What do you intend

to do?

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THE WITNESS: We are continuing to isolate substance X from water loading experiments; we are continuing to purify it using the techniques I have described; we obviously wish to identify this material.

THE COMMISSIONER: Well, there were two things as I understood it yesterday. The first one was the isolation of digoxin with substance X, so you can isolate substance X and you can also determine whether some substance really is digoxin or not. The other aspect I found interesting was where you talked about the production of digoxin in the body, that is in the urine you spoke about the production of digoxin.

THE WITNESS: Well substance X -THE COMMISSIONER: Substance X or
something that registers.

THE WITNESS: Right.

THE COMMISSIONER: Are you continuing with that experiment?

THE WITNESS: Yes, those experiments are continuing.

MR. STRATHY: Q. Are you continuing to investigate, Doctor, will you be continuing to investigate the effect of these various resuscitation



Soldin, cr.ex. (Strathy)

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efforts on the possible generation of substance X?

A. Certainly.

Q. Thank you. Is there anything else you would like to add?

A. I think that is as far as I would like to go now, there are other things.

THE COMMISSIONER: You have been through that before.

MR. STRATHY: Given what my friend Mr. Roland said I am content to leave it at this point.

THE COMMISSIONER: Thank you. Mr.

Hunt.

CROSS-EXAMINATION BY MR. HUNT:

back to your evidence yesterday with respect to the death of Allana Miller. You indicated to Miss Cronk that you got a phone call from Dr. Costigan at about 2 or 3 o'clock in the morning and at that time he asked you if you would do an analysis on a sample of blood. I take it from your evidence you were not sure at that time whether Allana Miller was dead or not?

A. I can't recall. He might have told me she had died, I can't recall if he told me that or whether he mentioned she had an arrest.

Q. According to the chart she



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(Hunt)

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2	died, she was	pronounc	ed dead at 3:27 a.m., does
3	 that assist you		
4		Α.	As much as it assists you,
5	yes.		
6		Q.	Is that unusual that you would
7	get a call tha	t time o	f the night?
		A.	Yes, very unusual.
8		Q.	I take it you were asleep?
9		A.	Yes.
10		Q.	And you had to wake up and
11	answer the call?		
12		A.	Yes.
13		Q .	Did you make any notes of the
	call at that t	ime?	
14		Α.	No, I don't think I did; writte
15	notes you mean	?	
16		Q .	Yes.
17		A.	No.
18		Q.	So when was the next time you
19	heard somethin	g about	it?
20		A.	Well, it must have been somewha
	later when the	sample	had been obtained. Now, I can't
21	recall what ti	me that	was, these events occurred many
22	years ago as y	ou know,	but some time in the morning.
23		Q.	After you got up?



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A. Yes.

Q. I'm just going to read you a little bit of the evidence of Dr. Costigan about this, all right?

A. Sure.

MR. HUNT: Mr. Commissioner, this is Volume 45, beginning at page 70, about line 20, and this is during direct examination by Mr. Lamek.

"Q. Now, can we move forward, move on to an event later on in that week. We know that in the early hours of Saturday morning, March the 21st, a baby called Allana Miller died on Ward 4A. I don't believe, Doctor, that you had anything to do with the care and management of that child, am I right?

A. Yes.

Q. A Code 25 was called. Were you involved in the unsuccessful resuscitation attempt on that child?

A. No.

Q. All right. When did you learn of her death?

A. It was approximately maybe 7:30 on that Saturday morning, the



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"21st.

Q. Were you on duty that day?

A. No, no.

Q. Were you at the hospital when you found out about Allana Miller's death?

A. Yes. I had just dropped in my wife. She was working that day, she's a nurse in the Hospital.

Q. Your wife is a nurse at the Hospital?

A. Yes.

Q. Working the day shift that day?

A . Yes.

Q. So, you had driven her to the

Hospital?

A. And I had gone up to do some

work myself.

Q. All right. You had arrived

then, what, about 7 in the morning?

A. Yes. She had to start at

7:30, so, it was about 7, 7:15.

Q. All right. And was it shortly

after your arrival that you learned

of the death of Allana Miller?

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	"A.	Yes, I phoned Dr. Canny.
	Q.	Who is he, please?
	A.	Sorry, Dr. Canny is the
	Associat	te Chief Resident who was on
	call tha	at night.
	Q.	Yes. The preceding night?
	Α.	Yes, the preceding night.
	Q.	And was it from him that you
	learned	of the death of Baby Miller?
	A.	Yes."
	Now, sir	from that it would appear
that Dr. Costig	gan first	learned about the death of
Allana Miller	at 7:30 i	n the morning. Would you
agree with me i	t sounds	that way?
	A.	Yes.
	Q.	Then we have Dr. Carver's
evidence, and 1	am refe	erring to Volume 35 at page
6829, Mr. Commi	ssioner,	where he has just finished
talking about a	a meeting	that was held at the
Coroner's offic	ce on the	e Saturday afternoon, that is

evidence, and I 6829, Mr. Commis talking about a Coroner's office the afternoon of the 21st:

> "Q. I understand you did not learn of the death of Allana Miller until you returned to the Hospital after the meeting of March 21st?





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"A. That is correct. I went from that meeting to the Hospital and then Dr. Costigan met me in my office and told me that another child, Allana Miller, had died on the ward, that digoxin level had been drawn but because of the weekend there was going to be a delay in determining this. I requested that special procedures be instituted so that that digoxin level be developed as quickly as possible. I think I specifically asked him to call Dr. Soldin and stated that

we needed this right away."



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Do you agree with me it would appear that Dr. Carver's recollection is he told Dr. Costigan to give you a call sometime Saturday afternoon?

A. That's what it sounds

like.

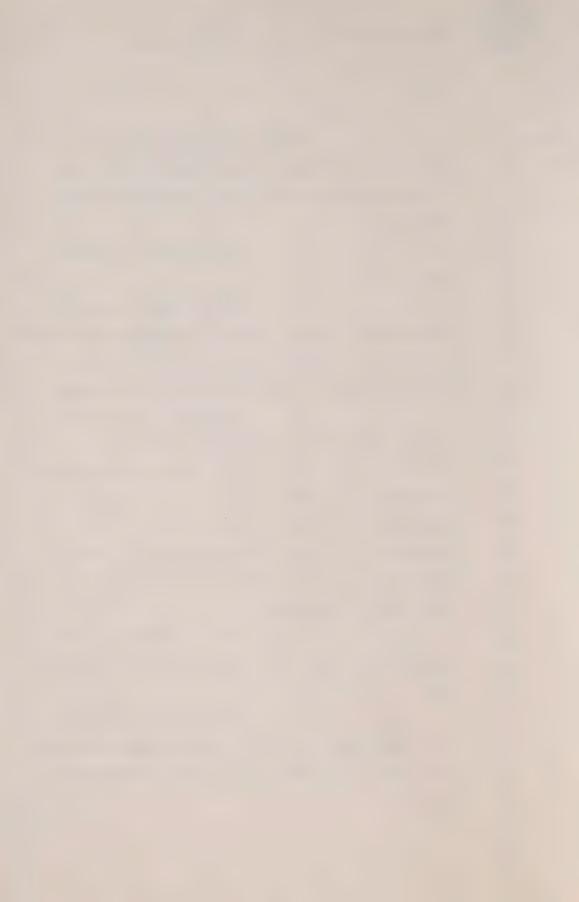
Q. Well, would you agree with me then there is no way Dr. Costigan was calling you at two or three in the morning on Saturday morning to tell you anything about Allana Miller?

A. From what you've read me his recollection is different from mine.

Q. All right. So, there is no doubt in your mind at all that two or three in the morning on Friday you got a call from Dr. Costigan -- I'm sorry, Saturday morning, two or three in the morning on Saturday morning you got a call from Dr. Costigan?

A. Well, I thought it was Dr. Costigan. Maybe I am in error but I thought it was.

Q. All right. Well then, let us see what you are in no doubt about. You are in no doubt you got a call at two or three in the morning?



Soldin cr.ex. (Hunt)

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A. Yes.

Q. No question about that

at all?

A. No question about that.

Q. So, if it wasn't Dr.

Costigan there was some other doctor who called you at two or three in the morning on Saturday morning to ask you whether you could do a digoxin level on the blood of Allana Miller?

A. Right.

Q. All right. We don't know who that doctor is but it is a doctor that obviously had something to do with Allana Miller and was concerned about digoxin and concerned about her blood level, the blood level of digoxin?

A. Yes.

Q. That was two or three

in the morning on Saturday morning?

A. Yes.

Q. All right.

THE COMMISSIONER: I take it this

could not have been Cook on Sunday morning?

THE WITNESS: No. No, I recollect

I had two phone calls in the early hours in the morning. One was on Cook and one was on Allana



Soldin cr.ex. (Hunt)

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Miller.

MR. HUNT: Q. Now, yesterday as well, sir, you told us about your analysis of some IV fluid. I believe this was with respect to the case of Justin Cook?

A. Yes.

Q. You gave the results of your analysis of the fluid and you indicated that the results as far as you were concerned, page 1334, ruled out the possibility that digoxin had been administered in the IV fluid. Would you like me to read you the question and answer?

A. Right.

Q. I'm looking at page --

A. No, I understand, you

don't have to read it.

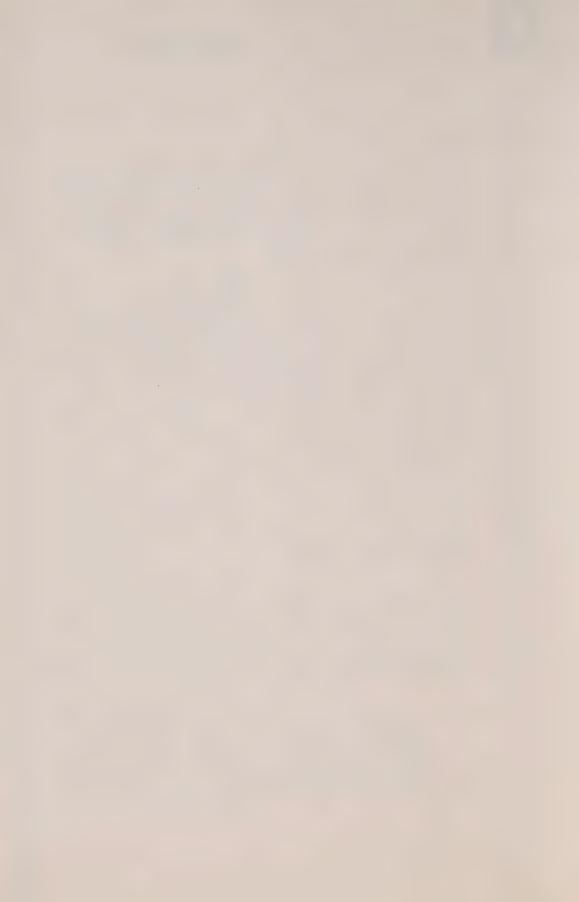
Q. Oh, do you, all right.

So, your testing of that fluid, as far as you were concerned, ruled out the administration, or the possible administration of digoxin by the IV fluid?

A. In that bag, yes.

Q. And you qualified that by going on to say that it was your understanding that the IV fluid that you tested was from the bag?

A. Right.



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Q. All right. And you agreed that, if we are talking about the line we

> A. Yes.

are into a different thing altogether?

Q. All right. Now, are you familiar at all with an IV fluid setup? It has the bag on a little stand.

> Somewhat, yes. A.

And usually the bag, the 0. fluid from the bag drips into a little bottle affair at the top I think called a buretrol.

> Α. Yes.

0. And then it goes down into the line and there is a little valve. There is a gap between the top of the bag and the fluid that is in the buretrol where it drips in, is that right?

> Yes. Α.

An down the line there are a number of entries on the line called ports. If one was to be of a mind to put something in an IV bag, I take it one has to take the bag down off the little stand that it is on and remove this connection from the top of it, that is where the line joins the bag and then put whatever it is into the bag and reinsert the connection at the top and



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put the bag back up on the little rack. Would that be a fair understanding of how one would put something into the bag?

A. I think one could just inject it into the bag if one wanted to.

Q. Right through the side of the bag?

A. Right through the side.

Q. In which case you might not have a leak all over the place I guess?

A. You might not.

Q. All right. Another way of injecting something by means of the IV fluid would then be to just take a syringe and put it in one of the little ports?

A. Right.

Q. And just squirt it in?

A. Yes.

Q. And the ports run down the line all the way down to somewhere close to

where it enters the patient?

A. Yes.

Q. I take it as between the two procedures if somebody was of a mind to give a patient something and they wanted to do it quickly,



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the easiest thing to do, the fastest thing to do would be to just inject your syringe into the little port and squirt the liquid in?

A. Yes.

Q. Because otherwise you are into this messy situation of having to take the bag down and put it in there?

A. Yes.

Q. So, really, the fact that you reject the possibility of the digoxin being administered by means of the fluid in the bag, that is only half the question as far as we are concerned, I appreciate that?

A. Certainly, yes.

Q. And it may be in terms of trying to decide whether or not digoxin was administered by the IV fluid we have to look at the other route which is through the line itself?

A. Yes.

Q. And it may well be that if somebody was of a mind to do it that is perhaps the best route to do it, or at least the better of the routes to do it. Would you agree with that?

A. Yes.

Q. Now, if I could deal for a



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E7	2	moment with your research, sir, in the Substance X.
	3	You indicated, I think, that this began about five
	4	months ago.
	5	A. I became quite heavily
	6	involved in this project about five months ago.
		Q. When would that be, in May?
	7	A. In May, yes.
	8	Q. So, that was after this
	9	Commission was called?
	10	A. After this Commission was
	11	called, yes.
	12	Q. Which was in April.
		A. Before I had appeared in
	13	it.
	14	Q. Oh, yes, the Commission
	15	didn't start hearings until late June.
	16	A. Yes.
	17	Q. So, do I take it from that
	18	that the project had something to do with the
	19	calling of the Commission?
	1	A. I don't think there is
	20	any connection whatsoever.
-	21	THE COMMISSIONER: It's the other
:	22	way around, surely.
	23	MR. HUNT: I beg your pardon?
:	24	



what I meant.

right.

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THE COMMISSIONER: It is the other way around, surely. The Commission had something to do with the research.

MR. HUNT: Well, I think that is

THE COMMISSIONER: Oh, I see, all

MR. HUNT: Let me try it a different way, Mr. Commissioner.

Q. Did the calling of this Commission in April in any way have anything to do with your involvement in the research project beginning in May?

A. I don't think there was any connection, no. Not in my mind anyway.

Q. Not in your mind?

A. Maybe in yours but not in

mine.

Q. Well, I am just trying to see whether there was because you see I have an open mind at this point. When was the idea to conduct this research project, when did it come to somebody first?

A. I think that is a very difficult question to answer. We have had anomalies



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maybe --

with digoxin measurement at the Hospital that I have been aware of for quite a long time, way before this. These anomalies obviously needed some research to sort them out. We were measuring digoxin in certain neonates. We were finding digoxin concentrations in neonates that were not receiving digoxin and this needed sorting out.

So, what compounds were causing these problems needed to be addressed and, you know, these ideas formulated over time.

Q. All right. Well, I think

A. So, I can't tell you exactly when, you know, on Tuesday morning, April 1, 1980 I had this brainwave, that didn't happen.

Q. Was it your idea to start the research project and get it rolling?

A. Well, Dr. Goldberg, who is our Biochemist in Chief, in discussions I had with him, he indicated that he thought this was an area of great interest and that we could well do some research in this area in the Biochemistry Department as such.

- Q. All right.
- A. We should look at that.



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So, he was very supportive of work in this particular area.

There is nothing sinister Q. about my question with respect to the timing of it, but certainly nobody is going to suggest there was anything wrong with starting it after the Commission had been called. But it would appear that these matters that are the subject of your research didn't become sufficiently important to actually undertake the research into them until the Commission had been called.

MR. ROLAND: That's a conclusion my friend draws. If my friend wants to know how it began, why doesn't he just ask the doctor.

> THE COMMISSIONER: I thought he did. MR. HUNT: I did, about ten

questions ago.

MR. ROLAND: He keeps suggesting things, like did this Commission have some influence or they weren't sufficiently important before this time. If you would just put the question.

THE COMMISSIONER: Well, I think he did though.

MR. ROLAND: If he just would put the question how it came about, he would answer it.



THE COMMISSIONER: I think he is

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trying to get the answer. Perhaps now that Mr. Roland has put the question, perhaps now you can answer it, do you think. What prompted it?

THE WITNESS: Many things prompted

One was, I have been trying to tell you, when we found digoxin measurements in patients that were not on digoxin. That was a key finding. It led to this research. I would say that the momentum of the research really picked up in May. At the beginning of May I wrote to Dr. Kuksis, who is one of the scientists at the Best Institute and he is an expert in mass spectrometry and I indicated, written at the beginning of May, that I would like to undertake this project, a collaborative project with him and that that project would involve highperformance liquid chromatography, separation of digoxin and Substance X. Identification of these two by mass spec. after we've carried out -- it would involve a lot more, it would involve the clinical pharmacology of Substance X, et cetera. This is all in the letter which I wrote to Dr. Kuksis dated early May. There are a number of problems when you start off a project of that type.

MR. HUNT: Q. Well, I don't want



some time.

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to get into problems just yet. I take it that what you are saying is that the basis of the research, the questions that it looks into are questions that didn't just crop up in May, they had come to you over a period of time?

> Α. They had incubated for

Q. All right. And there would have been nothing to prevent the research project starting in March or February or the year before if you had decided it was appropriate to do it?

Well, the evidence built up slowly. We found elevated digoxins, I think it was in January on Ward 7C/D when we screened all those kids that had been given epinephrine. So, I think that was in January that was really the major tip-off for us.

> That was 1982? Q.

Yes. A.

Ω. All right. So, we are

'83 now.

So, that was really the A.

major tip-off.

That is fair enough. My 0.

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point is, there was nothing that would have prevented the project from sort of being undertaken any time after that right up until May of '83?

No, it could have started . A. in '82, you're quite right.

So, was there something that happened then in '83, in April of '83 that caused the project to begin in May?

> Well, you are suggesting A.

Well, I am asking you, Q.

A. No, I just wrote this

there was.

sir.

letter.

0. It seems coincidental. I tell you I am not suggesting anything sinister about it but it seems coincidental and maybe that is all it is, but I am just asking, is there any relationship between the two, the project and the Commission?

Well, I can't give it Α. All I can say is in early May I wrote this to you. I wrote it. I had discussions with Dr. letter. Goldberg who was very enthusiastic about us getting involved in a digoxin project.



I guess?

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Q. All right. Now, your research has gone on from May right up until today,

> Right. Α.





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2	ρ,	I guess you are getting infor-
3	mation all the time?	
4	A.	Yes.
5	Q.	Last night you probably got
	information, did you?	
6	A.	This morning, yes.
7	Q.	This morning?
8	A.	Yes.
9	Q.	So we are really at the front
10	of the whole research	project right here and now,
11	aren't we?	
12	Α.	No, I am. You aren't.
	Q.	That is right, sir. Well, you
13	THE CO	MMISSIONER: Well, we might get

Soldin, cr.ex.

(Hunt)

credit for a little push, I don't know. MR. HUNT: Q. Over that five months

then, sir, you have isolated Substance X?

We have isolated a material, yes, which you can call Substance X.

Q. Well, when we talk about Substance X I guess we are using it in terms of the endogenous digoxinlike substance that was found in babies and reported to us, the Commission,

by Dr. Seccombe back in June or July?

A. Yes.

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1 2 Q. Now are we talking about the same Substance X? 3 I don't know. 4 I see. So you have isolated 5 another substance? 6 A. I have isolated a substance 7 from the urine of patients who are given a water load. 8 Q. Yes. 9 Of people who are given a water load. Not patients. 10 All right. 11 Who are normal adults. 12 Have you isolated the same 13 substance in babies? 14 No, I haven't. A. 15 Well then I take it --0. 16 Are you saying have I purified the substance from the blood of babies? 17 0. Yes. 18 No. A. 19 No. All right, and have you 20 purified the substance from the tissue of babies? 21 No. Well then your request yesterday 22 for the samples I take it was to allow you to see what 23



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you could do with them within the parameters of your research project as it stands right now?

A. Certainly, yes.

Q. When you indicated that, and I used the word this morning because I took it from your statement that you made yesterday that you have developed assays for the measurement of digoxin by liquid chromatography as well as by mass spectrometry that definitively show that this compound is digoxin and cannot be anything else.

I take it that is only part of your total research project, that aspect that you referred to yesterday?

A. Right.

Q. Well, is what you asked us for then you want the samples back so that you can pursue your research with the samples?

A. My research involves essentially Substance X, what it is, what it does, and its purification and properties. I am very interested in that area. I think that this Commission --

Q. I am sorry. I take it you haven't done it yet on the blood or the tissue of babies?

A. No, I have not.

Q. All right. What you want from us,





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from the Commission, is the tissue and blood samples of any of the babies that are still available. And I am putting it to you that you want those, and I am not suggesting anything sinister here, but I am putting to you you want those to work on for the purposes of your research?

Well, I think the Commission is going to at some point have to address the issue of --Sir, could you just answer that question.

I am trying to answer the A. question.

Does it admit of a yes or no answer? You want those samples for the purposes of --

> No, I --A.

-- of doing your research? 0.

No, I disagree because my research

is as I said associated with Substance X.

Here we are looking at another question and the question is what this Commission is all about, what did these children have, what is this they had? Did they receive digoxin or is this an endogenous material such as Substance X?

Now it so happens that our resarch on Substance X has led us to develop procedures which



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can separate Substance X from digoxin and can definitively identify both these materials, Substance X and digoxin.

 \mathfrak{Q} . You have done that in the urine of patients who were water loaded?

A. Right. When we say Substance X again, I emphasize that this need not necessarily be the same material that gives rise to digoxin activity in blood. It probably is very similar. It could be the same.

Q. Sir, isn't it obvious, and again

I am not suggesting anything untoward here, but you
want the samples that the police and the Centre for

Forensic Science have so that you can run the test
that your research project has developed, and that you
are working with now and you are still in the stage
where you don't want to talk about. You want to see
what you get?

A. Let me put it another way, I don't mind not getting these samples --

Q. Well, we are not saying that we -

A. Well, bet me finish, please.

I don't mind not getting these

samples. If the Commission wants to arrive at some conclusion on as to whether this is Substance X and



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digoxin, they may approach us and I will be happy to help them with that. But I am not pressing for these samples. I just indicated that we may be able to help you in this area.

Q. Well, if some other organization that is interested in the same subjects, the same issues as you come to the Commission and ask for the samples to use then, is there any way we can sort of weigh out the merits of the various research groups that we should dispense the samples to?

You can do whatever you like. THE COMMISSIONER: Well, no, but just try to help us, Doctor. Don't get into a row with counsel.

Can you, if you get a sample, can you tell us or do you think you can tell us how much of what is in it is digoxin and how much of it is Substance X?

Do you think you can do that? Have you donethat on any serum so far from anybody? THE WITNESS: We have purified --THE COMMISSIONER: Adults or child or

anyone?

THE WITNESS: We have purified samples of Substance X from urine as I have indicated.





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There isn't enough Substance X usually in serum for serum to be a good source.

As you know, patients with renal failure or premature infants might have Substance X at concentrations which correlated at no greater than 4 nanograms per millilitre of dogoxin. In other words very low concentrations.

I am merely giving water load experiments. One can isolate digoxinlike activity in much greater amounts from urine very easily, painlessly, and this material can then be purified and Substance the dig.-like material can be identified and we have done that.

Whether this Commission decides to give us tissues or blood samples is their, you know, it is something in their judgment that they can do or not do. I really don't mind what they do.

MR. HUNT: Well, the Commissioner's question was whether you had ever separated the Substance X in serum, blood serum?

THE WITNESS: I said no.

MR. HUNT: Q. All right.

Three times.

And I take it you haven't

separated it in tissue either?



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A. No.

Q. All right. So that to that extent what would come of your testing these samples is speculative and as it involves the application of your research to something that has never been applied to before?

A. But that is the nature of this proceeding. I mean you have got to find out at some point whether these samples contain digoxin or whether they contain Substance X.

Q. Well --

A. At some point this Commission is going to have to face that.

Q. And maybe, sir, at some --

A. Now I don't mind which lab they give the samples to. It makes no difference as long as they give it to a good lab, but at some point somebody is going to have to analyze these samples and assess whether the samples contain digoxin or Substance X.

Q. Well, sir, you wouldn't want to use up all of the samples in an experimental phase of working out a methodology, would you?

A. I certainly wouldn't. In fact I don't want to get these samples for quite a while yet.



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that is fine.

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Q. Well, you see the trouble I am having is I took from your unsolicited statement to the Commission at the close of the evidence yesterday that you had worked out a tried and true and tested procedure that was going to give us the definitive answer with respect to Substance X and digoxin in the tissues and serum samples that may be left.

Now that may be my fault, but if ${\tt I}$ took that from what you said it appears now that ${\tt I}$ am wrong?

A. We could try and help you in that way.

Q. And --

A. If you wish. If you don't wish,

Q. Sir, you can appreciate, though, can you, that we have to be relatively careful about what we do with the samples of tissue and serum that may be remaining?

You asked us yesterday not to break them up and give them out to individual groups?

A. Right.

Q. So I take it you appreciate we have to be careful what we do with them?

A. Well --



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Just that question.

A. I would hope that you would be more careful than you have been perhaps in the past.

Q. Oh, I see.

THE COMMISSIONER: What are you referring to now?

MR. HUNT: Q. Sorry. What are you referring to now, sir?

THE COMMISSIONER: Give me a chance to think about that now. Now whom were you referring to who has not been careful?

THE WITNESS: Well, it depends. You have crucial material. Material that one has to deal with very carefully.

MR. HUNT: Q. We appreciate that. Just answer the Commissioner's question. Where haven't we been careful in the past?

A. Well, I am somewhat critical of the way some of these samples were analyzed as I have already stated.

Q. Yes. You set out - the last time you set out - the last time you were here and I can read you the pages where you set out the concerns you had, and you indicated you didn't know enough about the procedure then to comment any further.



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- Q. And we have what you said today.
- A. And I am still as critical as
 - Q. Fair enough. And then --
 - A. And on those grounds I made today
- Q. And based on that you are saying we haven't been cautious or there hasn't been caution exercised in the handling of samples?
- A. You seem to be well, you seem to be more cautious when it comesto thinking about giving samples to our lab, yes.
- Q. Well, sorry, I don't understand that at all. What do you mean we seem to be more cautious when it comes to thinking of giving samples to your lab?
 - A. I mean exactly what I say.
- Q. Well, I don't understand it. Can you explain it?

THE COMMISSIONER: I don't either,

Doctor. That doesn't help us. What is it? What do
you mean?

THE WITNESS: Well, there was an inference that we wouldn't be analyzing these materials appropriately. You have made that inference.





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THE COMMISSIONER: I thought the inference was that the material might be used up without any results coming from it and then we would have nothing to experiment on.

THE WITNESS: Right. And that is always a possibility. And would caution you against that, but there is nothing that I or any other analyst --

THE COMMISSIONER: Well --

THE WITNESS: You know they cannot guarantee getting results on these samples.

MR. HUNT: Q. When was the inference made by me or anybody else that those shouldn't be given to your lab for any particular reason?

A. Something that I have taken from your questions.

Q. I see. So from the questions I have asked you here this morning that is what you have taken?

A. Right.

Q. You agree that we are concerned as the Commissioner pointed out with the materials being used up?

A. Yes. I am concerned too about



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Q. Well, I guess to go back to my original question a few moments ago if I take from what you said yesterday that you had a tried and true procedure worked out through your research that was going to give us the definitive answer as to whether or not the tissues and serum that we had contain digoxin or Substance X I was wrong?

A. Well, we have never isolated Substance X from tissues or serum. We would have to try and do that. We have never done that.

Q. Wouldn't you feel a lot better about the procedure if you tried that and had done it and you could come to us and say here are our results from trying it on tissue and serum in babies over the last number of weeks or whatever?

A. But you would have to find a patient who had values of around 70, number one.

These patients --

Q. No question, sir. It may be difficult for you to find --

A. Impossible to find.

Q. But nonetheless wouldn't you feel a lot more comfortable with your procedure if you had tried it in those situations?

A. Yes.





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I have.

Mr. Hunt.

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Q. And then you came and told us that you could give us the definitive answer?

A. Yes.

MR. HUNT: Those are all the questions

THE COMMISSIONER: Yes. Thank you,

Mr. Young?

MR. YOUNG: Thank you, Mr. Commissioner

CROSS-EXAMINATION BY MR. YOUNG:

Q. Doctor, I understand that you told us yesterday and you told Mr. Hunt this morning that the highest level of this Substance X, this endogenous substance, that anyone has recorded to date is approximately 4 nanograms per millilitre?

A. Right.

Q. And I think you told us that you are now able, and I am being a little repetitive with respect to Mr. Hunt's last questions, but correct me if I am wrong, you are able to identify this Substance X to isolate it with respect to urine samples. Is that correct?

A. That is correct, yes.





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		Ω.	And when did you become able
to do	that,	Doctor,	was it approximately 10 days ago?
		Α.	No. it has been an ongoing

study, it has taken many months to develop. All I can say is over the last five months we have developed a procedure which approximately 10 days ago we gave a sample for mass spectrometry analysis.

And that is where you became a little more certain that you could isolate this particular substance?

> Α. Right.

O. Doctor, I also understand you have been guite active in the therapeutic drug monitoring program at the Hospital?

> Α. Yes.

And in the course of that 0. program I take it you have done many, many digoxin assays?

> Yes. Α.

Doctor, I further understand 0. that since March of 1981 digoxin assays, postmortem digoxin assays have been done on every child who is autopsied at the Hospital for Sick Children, I imagine you are aware of that, are you not? That is the statement Dr. Cutz made here last week, or a week



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prior to that. I can get it and read it to you.

A. No, I believe what you say.

I thought I had somewhat different information from

Dr. Phillips, but anyway.

Q. It was Dr. Cutz that said that, but what information do you have?

A. I wasn't sure that we had autopsies happen on every death at the Hospital.

You can ask Dr. Phillips, I mean you will get it from him rather than from me.

 Ω . We will do that. What criteria did you think was used in order to decide --

A. I think in almost all the deaths they did have, certainly the vast majority.

Q. Doctor, you have some involvement with the testing of these samples that are taken during autopsy, you had more involvement at various times?

A. Right.

Q. But you still had some involvement, and you did have some involvement and you probably had been involved in, would it be correct to say dozens or hundreds of postmortem, tests of postmortem blood samples?

A. I think that since this time



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period there have been over 700 altogether.

- Q. That is since March of 1981?
- A. Yes.
- Q. Doctor, these children that are autopsied at the Hospital some of these children clearly would have been on digoxin during their lifetime?
 - A. Yes.
 - Q. And some of them wouldn't have

been?

- A. Right.
- Q. Some of them would have been

from the cardiac ward?

- A. Right.
- Ω . And some of them wouldn't have

been?

- A. Right.
- Q. Some of these children would likely have been the subject of resuscitation, unsuccessful resuscitation attempts prior to their

death, would you expect that to be true?

- A. Yes.
- Q. And during these resuscitation attempts I imagine that we can safely assume that

electric shock was used and large amounts of



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adrenalin	were	used	in	order	to	try	to	bring	these
children	back t	o life	e?						

- A. Yes, some of those.
- Q. Yes, certainly not in all of
- A. In a few maybe.
- Ω. Doctor, before we leave that,
 I understand you were involved on testing of Baby
 Murphy who died in April of 1983, is that correct?
 - A. Yes.
- Ω . And this child had postmortem digoxin levels, you can help me, Doctor, I think it was in the neighbourhood of 20 or 30 nanograms per millilitre, is that right?
 - A. Right.
- Q. And there was a coroner's inquest with respect to this child's death?
 - A. Yes.
- Q. And the conclusion was reached as to this child's cause of death I believe?
 - A. Yes.
- Q. You told Miss Cronk yesterday and you told the Commissioner that prior to the end of March of 1981 I believe you said you had never seen a digoxin level of 70 or greater?



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 Ω . And Doctor, in all of the many hundreds of tests that you have done prior to March 1981 have you ever seen a digoxin level of 70 or greater?

- A. Since?
- Yes, since March of 1981?
- A. No.
- Q. And have you seen a digoxin

level of 50 or greater since March of 1981?

- A. Due to contamination that is
- Q. And you told us about that.
- A. Apart from that.
- Q. You have not?
- A. No.
- Q. What is the highest digoxin

level?

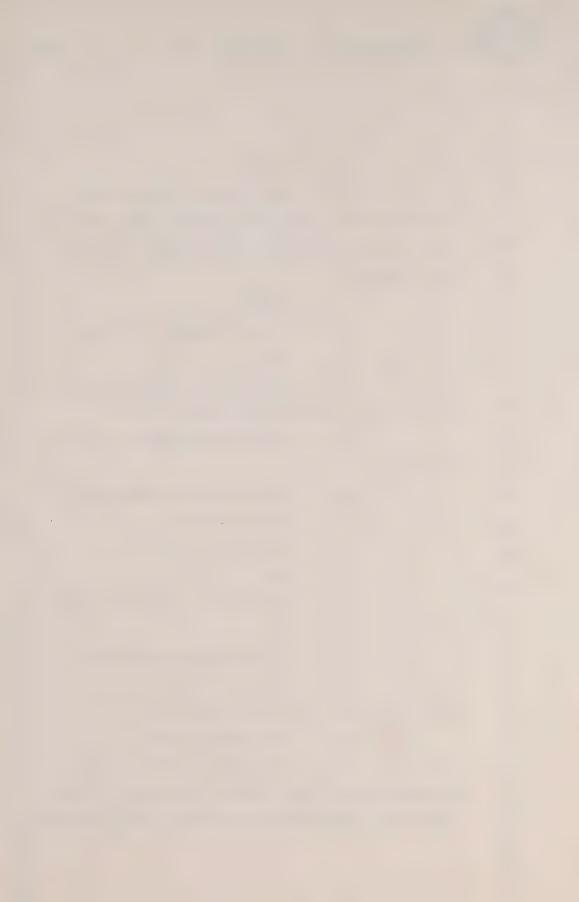
possible.

- A. I would have to check that.
- Q. We have already spoken about

Murphy, but can you give me a rough idea?

- A. It would be under 20.
- Q. And Doctor, some of these

children who have been tested, whose blood has been tested after the autopsy went through this electrical



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shock and high doses of adrenalin and underwent all of these procedures and some of them were on digoxin as we discussed; would you not agree with me? And I ask you to consider one more point and we just discussed that, the fact that levels of substance X have only been recorded up to 4 nanograms per millilitre. Would it not be true that in view of all these facts it is rather unlikely that substance X is going to explain away the 72's and the 78's that we saw in the Hospital in March of 1981?

A. Unlikely, I can't give you statistical - it is possible, but it is unlikely.

 Ω . It is rather unlikely; it is quite unlikely?

- A. I think it is possible.
- Q. How would you rate that possibility, do you think there's a good possibility, Doctor, a good chance?
- A. I don't want to rate it. I think there is a possibility and I don't think it is that minor a possibility.
- Ω. Well, Doctor, can you tell me how you think these levels can be explained away by substance X after all that we have discussed? I mean what is going to be the missing factor, what do you



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suspect to be the missing factor? You suggested yesterday it might the resuscitation attempts, and we have already spoken about the fact that many of the children, some of the children that you have tested over the last two years, two and a half years likely underwent such resuscitation attempts?

Yes. We are walking on new ground yet as I am sure you are aware, and therefore one has to be cautious about saying that something could not give rise to a value of 70 or 80. I will not say that, I think it possibly could. All I am saying is it possibly could, I'm not saying it did, I am saying it possibly could.

Can you help us with how that might happen with your present state of knowledge, do you have any idea about what extra factor might be in there?

One could surmise a million Α. different things. Substance X may be a hormone which is present in a particular tissue and if you get breakdown of that tissue substance X might be released in amounts sufficient to give you - it is conceivable in amounts conceivable to give you values of 70 or 80.

> But of all the children who have Q.



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died at the Hospital for Sick Children since March of 1981 that has never happened?

A. That is correct.

MR. YOUNG: Thank you, Doctor.

THE COMMISSIONER: Yes. Now, Miss

Jackman.

MS. JACKMAN: No questions,

Mr. Commissioner.

THE COMMISSIONER: Mr. Olah?

MR. OLAH: I do, but I will be a

while. Would you like to take a break now or would you like me to commence?

THE COMMISSIONER: Whatever you wish

I suppose.

MR. OLAH: I will be a while.

THE COMMISSIONER: All right, we will

take 20 minutes.

---Short recess.



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THE COMMISSIONER: Yes, Mr. Olah.

MR. OLAH: Miss Jackman would like to ask some questions, Mr. Commissioner.

THE COMMISSIONER: Yes, all right.

Miss Jackman.

CROSS-EXAMINATION BY MS. JACKMAN:

Doctor, I have just a few questions.

Doctor, when you testified previously on July 7th you mentioned that Dr. John Gault in Newfoundland had been conducting studies. Have you found out the results of those studies?

A. Well, I have some of his data, yes, the data that he has published, I have read that.

Q. Can you make a copy of the data that he has published and make it available to us?

> Certainly, yes. A.

Then, secondly, you mentioned Q. that Candy Cheong had done some of the assay runs on the Miller sample?

> Right. A.

Q. And that on the Sunday

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following another person in the lab had done some of the assay runs?

A. Yes.

Q. You also stated that you had reviewed the procedures that they had used. How did you review the procedures? Like, what does a review of their procedures entail?

A. Well, one looks at the curve, that standard curve, one looks at whether that is appropriate, one looks at the control values obtained.

Q. So, it is reading that they have written down?

A. No, it is reading what the standard curve - yes, it is reading the counts that one would get in a radioimmunoassay. We have been through this when we discussed what a radioimuunoassay was. It is a long time back. But you get different numbers of counts when you have different concentrations of digoxin in a sample. So, you would review that using standards and then you would review the results for the controls and then you would look at the results for tests.

Q. Then, Doctor, I understand that you were satisfied with the way those tests had been handled. I would like to know just a bit more.



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Do you know how long Candy Cheong, for instance, had been at the Hospital, how much experience she had had in doing those kinds of tests?

A. You had better ask Dr. Ellis, she works in his lab. She has been with us a long time.

Q. And the other technician?

A. Also a very long time. Both of them have been with us I think at least five years.

Q. And they have been doing these kinds of tests?

A. Yes.

Q. Throughout that time period?

A. Right.

MS. JACKMAN: Those are all the

questions I have.

THE COMMISSIONER: Thank you, Miss

Jackman.

Mr. Olah?

CROSS-EXAMINATION BY MR. OLAH:

Q. Doctor, I would like to follow up on some questions that were asked by Mr. Hunt.

First of all, I take it that the first indication you had of substance X, or something unusual occurring, was in January of 1982 when you



had the results of the digoxin test taken on Wards 7C and D, was it?

A. Right.

Q. And at that time there really wasn't any theoretical explanation for the phenomena that you observed. Am I correct in understanding that?

A. I would have to review the literature at the time. There were a few papers that were published around that time talking about endogenous digoxin like material.

- Q. All right.
- A. But apart from that.
- Q. That was a theory that really didn't have much currency or acceptance at that time, as I understand it?
 - A. Yes, I think you are right.
- Q. And, in fact, the development of this substance X theory occurred some time between January of 1982 and April of 1983 when Dr. Seccombe published his publication that we have seen?
 - A. Yes.
- Q. And I take it that it was in that environment of this developing controversy about substance X that you came up with a mode of



refining substance X?

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Yes.

And all that you are teiling this Commission is that you have developed a mode or a technique that is more specific than RIA for isolating substance X?

Yes, and differentiating it from digoxin.

That's right, because the 0. problem with the RIA system, as I understand it, is that it cannot distinguish, or we don't believe that it can distinguish between substance X and digoxin?

> Yes. Α.

And what this new mode that you have applied, which is a more developed or refined technology or application of technology allows the precise separation of digoxin and digoxin like substance such as substance X?

> Α. Yes.

So, what you are suggesting by the release of samples is really the application of the highest available technology known to mankind today in isolating or separating substance X from digoxin?

> I was suggesting that A. Yes.



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hopefully.

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that would be a way to differentiate between these two in these particular samples.

And that would hopefully forever 0. lay to rest any speculation or suggestion that these high readings are as a result of substance X or something digoxin like rather than digoxin. It possibly could ---

THE COMMISSIONER: It depends on which side you are on.

MR. OLAH: It depends. Well, it doesn't matter which side we are on, I guess, Mr. Commissioner.

THE COMMISSIONER: Well, you said

MR. OLAH: Hopefully, yes.

THE COMMISSIONER: Yes.

MR. OLAH: Well, let me recast the question, Doctor.

What this technique, the 0. application of this technique could do is to tell us whether in fact to what proportion substance X impacts on these readings?

Well, I think, you know, if A. successful, if one was given a tissue sample let us say from Justin Cook, a heart sample, and if we





measured, if we used these techniques to measure digoxin in that sample and if we found no digoxin to be present yet when we used the same techniques on other heart samples in patients that have been receiving digoxin and if we then found digoxin to be present in those other ones, we would then be able to say that the samples from Justin Cook didn't have any digoxin in them. We may as well be able to look for substance X because the procedures we have developed essentially enable us to look at both of these materials.

Q. Well, I am not sure I understand that, let me see if I do.

You have now developed, or you have successfully satisfied yourself that the process that you have applied can measure out digoxin or separate out digoxin and substance X. Am I correct?

- A. Yes, that is correct.
- Q. And that was on urine samples?
- A. We can separate out digoxin

in substance X.

Q. All right. And what in effect those most recent testing has done has satisfied you that the application of this liquid chromotography and mass spectrometry in fact works in separating out



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A. Yes.

Q. And so far it has been run on urine, as I understand it. You are going to have to say yes or no?

A. Yes.

Q. And the reason that urine was used is because you can get fairly high levels of substance X in urine?

A. It was a much, yes, the source was a good source to use to purify substance X from.

There is very little substance X present as we know in blood.

Q. In blood, all right. And now that the system or the technology is operating satisfactorily you want to move on or you think that you could move on to something different, a different mode or a different substance possibly containing substance X which would be blood or plasma?

A. Blood or plasma, depending on the concentration of substance X in that sample.

You know, it may or not be possible to do this particular series of experiments and that's why I am hesitant.

Q. That's the point I was coming



to. That's why you are hesitant. You're not sure to what extent substance X would be found in these samples of blood?

THE COMMISSIONER: But assuming it was there, surely that's the problem Assuming it is there, Doctor, would you have a problem in finding it in blood?

THE WITNESS: Well, it depends on the concentration at which it is there.

THE COMMISSIONER: Yes, but if it is a small concentration you would have trouble, is that correct?

THE WITNESS: Yes, I think we would have trouble if it was a low concentration and if it was a high concentration I think it would be much more easy.

THE COMMISSIONER: That wouldn't worry us because if it is a low concentration then it wouldn't be of importance but if it is a high concentration it would be of importance. You say that you think your system would detect high concentrations of substance X in blood?

THE WITNESS: I think it would, provided we had (a) a high concentration and (b) a big enough sample. So, I am sorry that I can't be



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more explicit than that at this point. We have never

done it from that source.

THE COMMISSIONER: Well now, I realize that I think you said yourself substance X, and maybe I am over-stating this, but it has never been found in concentrations, or seldom found in concentrations of higher than 4 nanograms?

THE WITNESS: Right.

THE COMMISSIONER: Would that be sufficient? Say 4 and 72, would that be sufficient? THE WITNESS: You're asking me to ---THE COMMISSIONER: If you have no idea whether it would or not, just say so.

THE WITNESS: I think it probably would be if the concentrations were around 72 and if the concentrations -- but it always depends on the volume of material you would give us.

THE COMMISSIONER: I see.

THE WITNESS: So, there are two factors here: one is concentration and the other is volume. If we were given a big enough sample with a high enough concentration I think we could use these techniques to separate.

MR. OLAH: Q. Well, on the converse side of the coin, Doctor, would it be fair to say



that if your system doesn't pick up substance X then we can be fairly certain that the reading is accurate in terms of digoxin and that it does not contain any digoxin like substances?

A. Well, I would be hesitant about that one. There may well be more, as you know, more than one compound which has dig. like activity.





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		ζ	2.		So	we	are	now	talking	about
substance	X,	Y	and	Z	poss	sibl	Ly?			

A. Right. There could well be a series of compounds.

Q. And is there any basis for suggesting that or is that just theoretical at this stage?

A. I usually - no, there is some basis for that.

Q. All right. Let's just go back to the question I asked you a moment ago: assuming that your instrumentation doesn't pick up any indication of substance X or possibly other digoxin-like substances, can we then fairly safely assume that the readings we have heard in evidence here can be relied upon as being digoxin and fairly accurate digoxin levels?

A. No. Yes, I am hesitant about the values that - about the interpretation of values that have been found.

Q. Well, I am somewhat at a loss and maybe you can tell me why you have that problem?

A. Well, the issue is - the problem is, as I said, a value of 72 nanograms per ml of digoxin is that really digoxin, and I have a problem



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saying that it definitely is.

0. Well --

It may be caused by substance X or Y or Z or whatever you want.

O. All right. But given the highest and most sophisticated mode of detection available to us today, which I understand is this new system that you have developed, there are only two possible alternatives: one is the application of your system reveals the presence of these substances, in which case we will be able to say to what extent it is accurate --

- Α. That is right.
- Q. Or alternatively, it doesn't detect it and then we can, can we not, readily say that it is in fact accurate because you have not been able to detect --
 - As long as --A.
 - 0. -- substance X, Y or Z?
 - As long as it detects digoxin,

yes.

The process has to detect either digoxin or substances X, Y, Z or any other dig. like material.

Q. Well, is there any doubt that



your process	in	fact	does	detect	digoxin?
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A. No. You can detect digoxin using this method.

Q. So that as long as you have got sufficient volume and a fairly high digoxin reading, if your system fails to detect digoxin-like substances X, Y or Z, then can we not be fairly certain that in fact readings we have are digoxin?

A. Yes. Under those circumstances, you can be sure they are.

Q. All right. So in fact if there are sufficient samples left, and I am just talking about blood at the present time, then your testing would help us either way because either it will detect high levels of substance X or Y or Z or it will not, and in which case we will be able to say it is digoxin and not some other substance.

A. If you detect digoxin you will be able to say it is digoxin. If you don't detect digoxin I think the question is still open.

Q. All right.

THE COMMISSIONER: Sorry. Could there be some question as to whether you would detect digoxin in this?

THE WITNESS: In patients who haven't



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received digoxin you may - if this whole reading is caused--

THE COMMISSIONER: No, but what about the readings that were done under your supervision?

Aren't they digoxin?

THE WITNESS: Yes, that is using either - that was using the radioimmunoassay procedure.

THE COMMISSIONER: But you now have some doubt about that system, the whole system?

THE WITNESS: Well, there is problems

of specificity with that system.

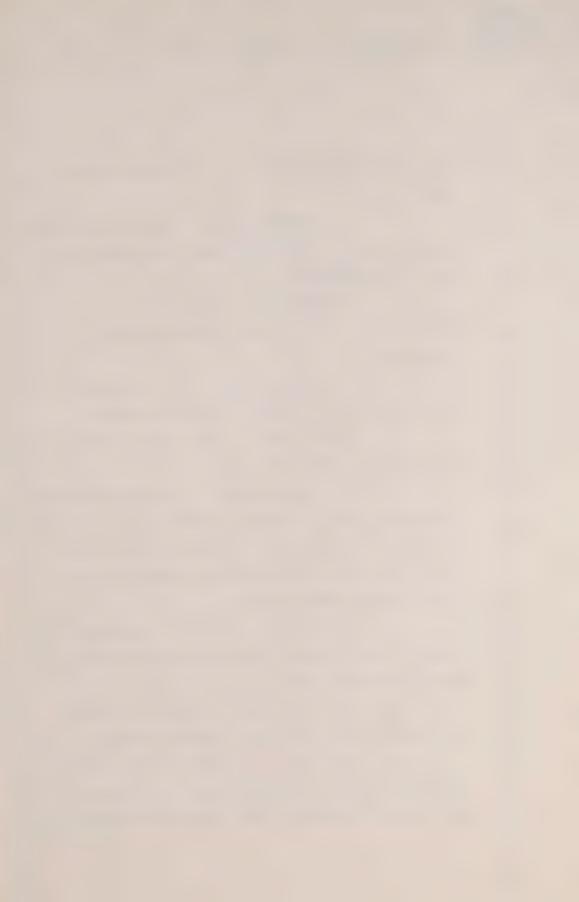
THE COMMISSIONER: I understand that, but what Mr. Olah is saying, you now tell us that you can isolate substance X. If you take that and you can do that, doesn't the remainder become digoxin?

Isn't the remainder digoxin?

THE WITNESS: The same procedure that we used to measure substance X can be used to measure digoxin. That is HPLC and mass spec.

If these infants were given digoxin we should therefore be able to detect digoxin.

MR. OLAH: Q. Fine. Let's use that example. What your technique does is it gives a very specific reading of the particular substance you



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are looking for? Right?

- A. Right.
- Q. All right. So if we were to give you a blood or plasma sample from, say, Justin Cook, and you looked for digoxin, and assume that there is high levels of digoxin there, you would be able to find it, would you not?
- A. I would be able to find it if it was there, yes.
- Q. And you would be able to measure the concentration? Right?
 - A. I think so. Well --
- Q. And then after you have measured that you would be certain, given the most sophisticated application of science today as to (a) that it is digoxin only, and the level that is contained in that? Correct?
- A. I think if one could rule I think we could definitively establish whether or not digoxin was present. Right. I think if substances X, Y and Z and possible others were not present, that one could assume that the radioimmunoassay result was accurate.
- Q. Okay. And conversely if you found high levels of X, Y or Z then that would cast



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great doubt on the readings we have got?

- A. Yes. Right.
- Q. So either mode would be very helpful to this Commission? Isn't that what you are saying?
 - A. That is what I am saying.
- Ω. And presumably because you have had the advantage of Mr. Cimbura's experimentation with respect to tissue you will be able to use his research and apply your specific testing mode and possibly come up with some sort of pretty precise measurement with respect to tissue? Is that what I am hearing?
- A. I think that if we worked together it could be done, yes. One could come up with a good procedure that would separate, isolate, purify and then measure digoxin in tissue samples using HPLC and mass spectrometry.
- Q. And what you are saying is that this would take time, but given the advances that you have uncovered it would give us a very definite idea with respect to tissue as to either the presence of digoxin or possibly digoxin-like substances?
 - A. I think it should, yes.
 - Q. By the way, have there been



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any recent developments, and I know we are on	the
frontiers of science these days, have there b	een any
further recent developments in this area of s	ubstance
X that you are aware of other than your own s	tudies?
Reports and the literature?	

- A. There is some yery recent abstracts, one by Galt, that you may or may not have which I will make available to you.
 - Ω. Perhaps you could assist us --
- A. And he isolated digoxin-like materials from patients with hypertension and normal individuals.
 - Q. Was that using RIA or --
- A. After using water load. Yes, using radioimmunoassay.
- Q. I guess what I am trying to get at at this stage is this: given the most recent knowledge as of today, first of all this Galt study, was this with neonates or with adult patients?
 - A. No, those were with adults.
- Q. Is there any recent change in the levels that have been reported by Dr. Seccombe in terms of levels to be found in blood or plasma as being the highest at about 4 nanograms?
 - A. Not that I am aware of, no.



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MR. OLAH: Thank you, Doctor. Those are the questions I have.

on this: you told me and I have a note here that
you would need a high concentration of substance X
and a high volume of blood to do your experiment.
But do you really need a high concentration of
substance X; if your system will differentiate
between substance X and digoxin why do you need to have
a Marge concentration?

THE WITNESS: Yes. I want to be sure that we will be able to tell you, yes, there is substance X present or yes, there is digoxin present.

THE COMMISSIONER: Yes.

both. The present purification procedure involves multiple HPLC runs and involves at the end direct probe mass spectrometry, possibly gas, GC mass spectrometry, so it is a long procedure, and you tend to lose material as you go along the procedure. You never have a recovery of a hundred per cent. So you always are losing material as you move with each step.



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Therefore, one would need to have adequate concentrations of those compounds present in the sample, I think, in order to definitively establish that they were there. If the concentrations were very low, I don't think we would be able to detect them.

THE COMMISSIONER: You wouldn't be able to detect them, but it wouldn't prevent you from detecting the digoxin?

THE WITNESS: Providing the digoxin was at a certain level, yes, above a certain concentration.

THE COMMISSIONER: Yes. All right.
Yes, Mr. Labow.

MR. LABOW: I have no questions,
Mr. Commissioner. Mr. Tobias and Mr. Shanahan

have told me they also have no questions.

THE COMMISSIONER: Now, Miss
Kitley, you were not around I think at the critical
moment, have you any questions?

 $\label{eq:MS.KITLEY: I gather I was missed} % \end{substrate} %$

THE COMMISSIONER: Yes. All right.

Mr. Roland.

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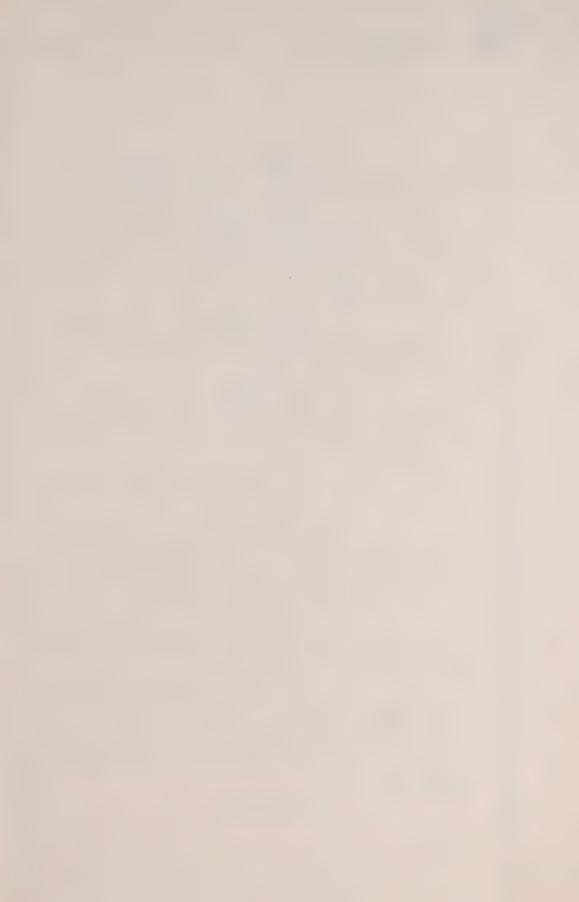
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Thank you.

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MR. ROLAND: I think, Mr. Commissioner, that you have, in the last few minutes, covered and understood the areas that I want to make sure are clear in terms of the method that Dr. Soldin is talking about.

RE-EXAMINATION BY MR. ROLAND:

Soldin, in order to conduct the study that you have told us about, using both HPLC and mass spectometry, you would require a fairly large sample of the substance, whether it is digoxin or Substance X, to begin with because the process, I understand, is one of concentrating that substance; that is, removing all other substances from the substance you are going to put through the mass spectograph?

A. Right.

O. Is that correct?

A. Yes.

Q. And that is why you run,

as you said, multiple HPLCs?

A. Right.

Q. And the reason you have used urine is because that is the way in which you

can gather fairly easily a sufficient quantity of the



yes.

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isolated substance?

A. Right.

Q. And I gather the reason you haven't tried it on babies, on serum of babies, is because, unless the concentration of the substance, be it digoxin or substance X, is extraordinarily high, you will not be able to isolate and separate out enough of the substance to run through your experiment?

A. You may not be able to,

Q. And I gather your experiments have been directed towards identifying the substances rather than quantifying them?

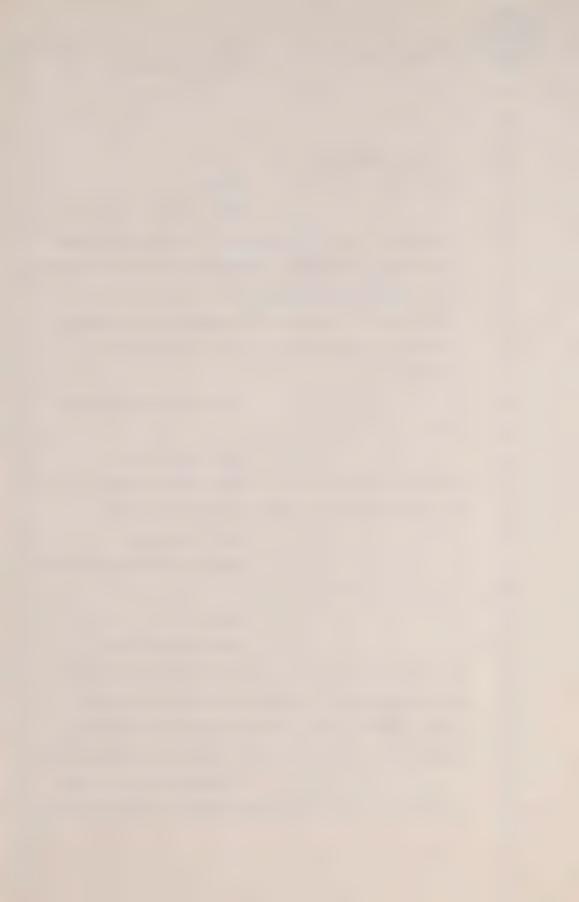
A. That is right.

Q. That is the whole direction of your experiments?

A. Yes.

Q. When you talk about using the tissues and the blood serum of the baby, Baby Cook and other babies that we are concerned with, you are talking about identifying digoxin or digoxinlike substances rather than quantifying them?

A. At this point, yes. At this point, one could always work out a quantitative



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procedure but, at the present time, we are talking about identification.

Q. Yes. And I gather that, today, you feel that your procedure that you have developed together with what you know about using samples of tissue, either by dehydrating them in order to then run them through the HPLC and separate out the substances, or by using some sort of a homogenation process, is sufficient for your purposes, for your experiments today, if you have enough quantities to identify in those substances, in that substance, whether or not you have digoxin or digoxinlike substances?

A. Yes, it should be.

Q. And it is for those

reasons, I take it, you thought it might be useful to the Commission, to aid the Commission, for you to attempt that process on what other tissue and serum samples may be available?

A. Right.

Q. Recognizing, I gather,

that you require a sufficient quantity of both
tissue or serum in order to concentrate the substance,
the digoxin or dig-like substance, to concentrate it
and give you thereafter a sufficient quantity to



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run through your mass spectogram process?

A. Right. Also recognizing that, before we ever embarked upon this, we would do numerous experiments of heart tissues in patients that have not received digoxin.

Q. Yes.

A. And we did numerous experiments on heart tissues of patients that had received digoxin.

Q. Yes.

A. So that we have a much better feeling for the reliability of the procedure were we to embark upon that line of investigation.

Q. And I gather, if we simply take a baby, take a neonate, for instance, with what has been detected as a therapeutic reading of, say, 2 or 1.5, and it has not been on digoxin, the kind of thing that we have heard about from Dr. Seccombe, and you took a sample -- and you wanted to try and take a sample of that baby's blood in order to determine whether or not substance X was present and try to identify substance X, that you wouldn't be able to obtain enough blood or blood serum to do your experiment?

A. Yes. I think there may be



a problem, but I don't know.

Q. In any event, when you were asked, have you isolated substance X in babies or in tissues, I gather what you have told us is that it is not that you haven't isolated them but you haven't tried to isolate them?

A. Yes.

Q. You haven't made that attempt yet; your experiments haven't dealt with that?

A. Our experiments haven't dealt with that, no. The concentrations, as you point out, are low, generally.

Q. Yes.

A. We would need a large volume, presumably, of blood, and we would exanguinate the patient, and it is not the way to go if you wish to purify compound X; it seems a very poor route to take.

Q. So, if you are provided with samples of tissue and blood of the babies that we are concerned with here and they are sufficient, there is sufficient quantity of those samples to conduct your identification method on, I take it that you will be not quantifying digoxin or Substance



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, you will be	rdeuctryrid	argoxin	or subs	stance X:
	Α.	Yes.	We would	l provide
a definitive	identification	on, firs	t of all	. It is
possible that	we could pro	ovide a	quantita	tive
estimate as w	ell, but one	would h	ave to w	ork that
011+				

Q. Have you developed a methodology yet to quantify it with the present process that you have?

A. We haven't evaluated the process quantitatively.

Q. Yes, all right.

THE COMMISSIONER: Do I understand that, if you were to have this experiment and if there were certainly 2 nanograms of digoxin plus X, you would be unable to tell us, first of all, how many nanograms there were of the two together nor of either one; is that right?

THE WITNESS: I think it would be, at this time, very difficult to put a number on that, yes.

THE COMMISSIONER: It seems to have been relatively easy for everybody to put a number on the total - we have got a whole book of them.



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THE WITNESS: Yes. You have a whole book of numbers, that's true. What they mean is another issue.

mean something; they surely mean D plus X, or perhaps D plus X plus Y plus X? Do they not mean that?

THE WITNESS: They mean --

THE COMMISSIONER: Do you mean this

means nothing at all?

THE WITNESS: No. I am saying that, under the conditions of radioimmunoassays carried out, we got certain values for digoxin; that doesn't mean that it was due to digoxin. It could be --

THE COMMISSIONER: I understand that. You are telling me now, or at least I think you are telling me - and please correct me if I have misunderstood you - that you cannot now, under your system, even get a total of what may or may not be pure digoxin; is that right? Am I misunderstanding you?

THE WITNESS: If you are asking me whether I can do it right now, today, the answer is that, using HPLC and mass spec., we have not



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employed these techniques from a quantitative aspect at the present time. We have done it from the aspect of being able to identify digoxin and identify Substance X.

THE COMMISSIONER: And in the present state of the art, if you got these samples, you would not be able to, provided there was any Substance X at all -- I am sorry. If you got these samples, whether there was or was not any Substance X, you wouldn't be able to tell us how much digoxin was in that sample?

THE WITNESS: I think, with a minimum of extra work, we would be able to do that. I haven't been trying to establish, up to this point, a procedure to quantify digoxin by HPLC and mass spec. What we have done up to this point in time is develop a procedure by HPLC and mass spec. which enables us to purefy Substance X and to identify what it is.

THE COMMISSIONER: But it doesn't tell you how much there is of it?

THE WITNESS: It doesn't tell you how much there is of it, right.

THE COMMISSIONER: And there are apparently a great many babies that do have



Soldin re.ex. (Roland)

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Substance X in small quantities and it really doesn't advance us very far?

THE WITNESS: It would tell you whether it is there or not.

MR. ROLAND: Q. And I take it, doctor, it would tell you whether digoxin was there or not?

- Α. Yes.
- 0. And you might -- the result of your mass spectrometry is that you may find digoxin alone, you may find substance X alone or you may find digoxin and substance X?

Yes, and the quantitative A. aspect would have to be worked out, and will be worked out in the future.

> 0. Yes.

Our work at this time is still not on this area. I mean, I have indicated to this Commission that we may be able to help in measuring digoxin or substance X in various samples but my research work doesn't involve that.

But I take it, doctor, 0. if we deal with the babies who at least we understand did not receive any therapeutic doses of digoxin, such as Baby Cook, you, if you had a



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a sufficient sample of either the tissue or blood serum from Baby Cook, you could tell us, indeed, whether or not there was digoxin or substance X or a combination of digoxin and substance X?

Yes. I think, with a Α. minimum amount of extra work, we could quantify it as well.

Now, in terms of the 0. studies that you have been asked about that began in May in a serious and concentrated way, can you tell us, was funding an issue in commencing the studies, continuing studies?

A. Yes, funding is always an issue, and it was a major issue in getting this project started.

Q. Did that affect the timing of the project?

> A. To a large extent it did,

And during the project, Q. have you had to carry on looking for additional funding to carry you through the project?

Yes. We are continuously Α. looking for additional funding.

MR. ROLAND: Thank you. Those are



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all the questions I have.

THE COMMISSIONER: Miss Cronk.

I am sorry, Miss Chown. This is your client.

MS. CHOWN: This is not my client

and I have no questions.

MS. CRONK: You were right the

first time, sir.

REDIRECT EXAMINATION BY MS. CRONK:

Q. Doctor, with respect to, dealing with the latter matter raised by Mr. Roland, the studies that you have been conducting, I would like to gain a better understanding, if I may, now that the matter has been raised, as to the exact nature of those studies, and it may well be that, at some subsequent date, if further results are available to you, you may be invited to reattend, as Mr. Roland suggested, by Commission Counsel or by the Hospital counsel, to discuss this, but then, again, this may not be the case. So, for present purposes, I would like to explore that with you.

First of all, doctor, we have heard in your prior evidence that, at the time with which we are concerned - July 1980 through to March 1981 - the RIA method was the only one being used in the Hospital for digoxin assays. Do I have that



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correctly?

Yes, you have that correct. 0. You told us, as well, about

your own subsequent involvement with the procedure known as the FPIA, the Fluorescent Polarization Immunoassay Technique, which is now used in the Hospital.

Α.

Α. Yes.

Do the tests which you have conducted, the water loading experiments that you have been describing, involve either of those two methods?

> Both of them, yes. Α.

Do I take it then, doctor, 0.

that you have, in addition to conducting these water loading experiments by using the HPLC and the MS method, as well run them on the RIA and as well run them on the FPIA method?

> Most certainly, yes. Α.

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Q. All right. So, you have used then all three techniques?

A. Right.

Q. All right. Doctor, with respect to the number of experiments, if you will, the number of assays run on the RIA technique, the water loading experiments, how many have you done since you commenced this work?

A. The number of assays run, single

Q. As part of this water loading

A. Yes.

Q. The research that you are doing?

A. Yes, that we are doing.

Q. Can you approximate it for us at all? Are we talking about 10, are we talking about 50, are we talking about a couple of hundred?

A. No, we are talking about something in the order of 10,000.

Q. 10,000 individual assays?

A. At least.

Q. On the RIA technique alone?

A. On the RIA and FPIA, yes.

Q. Well, I am sorry. My question



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was directed to the RIA.

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A. The RIA. At the moment we are switching to FPIA, as you know. So, we have done far fewer on RIA. We have done well over a thousand RIA I would think, certainly around 10,000 FPIA.

All right. Then guite separate and distinct from those two methodologies, you have as well run a number of assays using strictly the HPLC and the MS technique. Do I have that correctly?

We have, yes.

And then we are still talking about your water loading experiments. How many assays using that methodology have you run approximately since you commenced this research?

Well, you use the HPLC technique to purify Substance X and we have had to do multiple runs with that technique. We have done I would say close on a hundred runs at least, I would say. Somewhere around a hundred runs of HPLC. On mass spec. this is work done by Dr. Kuksis, he's done quite a bit. He has done mass spectro on samples which we have given him of digoxin, of the digoxin metabolites, of Substance X, and he has done them several times.

All right. Well now, Doctor, I am confused for an entirely new and different reason.



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You have referred to another doctor running tests using mass spectrometry.

A. Right.

Q. Do I take it then that you have not run assays since you commenced this research using that technique?

A. No. I know my limitations, I am not a mass spectrometrist and we have an expert in Toronto who is and Dr. Kuksis is.

Q. Is he at the Best Institute.

A. He's at the Best Institute.

Q. All right. I take it then that that flows from what I understood your previous evidence to be and, that is, that mass spectrometry had not been used for digoxin assays in The Hospital for Sick Children and it still isn't?

A. Well, Dr. Kuksis and I are working together on that and we are collaborating on this project together. I don't know where you draw the line. I think that he is involved in this project and the project is really taking place at Sick Children's.

Q. I understand, Doctor.

A. Yes.

In terms of the actual testing



that you personally have done then, I take it, you have told us about the test that you have run on the RIA methodology, you have told us about the experimental runs that you have done on the FPIA and you have as well done I think you said approximately 100 runs on the HPLC?

A. Right.

Q. All right. When you have finished any particular assay run on the HPLC do you then send that specimen to your colleague at the Best Institute so that it may then be run on MS?

 ${\tt A.}$ We send some of them, not all of them.

Q. So, we are not talking about a situation where those particular experiments are always done in combination. Any particular specimen is not always run on HPLC and then on MS?

A. No, no. What we have done essentially is in order to get sufficient material we have done multiple runs by HPLC. We have combined the fractions that have digoxin activity, we have then re-run them on HPLC, a different procedure, combined the fractions again, re-run them on HPLC, again a different procedure, combined the fractions, and this is continued until we are satisfied that we



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have a more or less pure form of Substance X, which we then give for either gas chromatography, mass spec. or for mass spec. and we have delivered several such samples.

Q. All right. Doctor, do I understand it then that in terms of these experiments and this research that you have been conducting, the very first step is to try and purify the substance by using the HPLC?

A. That's right.

Q. And it is only after you have done that to your satisfaction for the purposes of that particular run that you then turn to the RIA method or you then turn to the FPIA method, is that correct; in other words, does the HPLC run of the specimen precede any run of the specimen on the RIA?

A. Well, in order to detect -- at the moment our detecting device is either RIA or FPIA or mass spectrometry, so, it is one of those three. In order to detect Substance X we use RIA or FPIA. In other words, we measure the digoxinlike activity in all the column eluants.

Q. Yes, Doctor.

A. So, if we get, let's say every time we run a column we might have 40 different eluants



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24 25 that we collect. So, we would do 40 assays by FPIA on that particular run and we may or may not do it by RIA.

O. I see. But the first step in each case, in any case, whatever you subsequently do, is to try and purify the substance on the HPLC?

Right. So, we have used the HPLC first.

Q. All right. Then you would proceed to use one of the three other techniques, the RIA method, the FPIA method or you would send it to your colleague at the Best Institute to be run on mass spec.?

That's not quite right. We always start - we have done a lot of chromatographic purification but in order to identify the acts of fractions, in order to identify where Substance X is, any time we run every single chromatograph we have to measure the activity of digoxin and we measure that with FPIA currently.

Q. All right. But you have also done, you have told us, some on RIA?

We have done some on RIA.

And you have also sent some to your colleague at the Best Institute to be done on mass spec.?



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Only in the very pure form. A.

0. All right. So, far fewer have gone for that particular technique to be used, to your colleague at the Best Institute?

> A. That's right, yes.

All right. May we talk now about the specimens themselves, Doctor, and the patient, at least the sampling population if we may.

As I understand your responses to Mr. Strathy yesterday you told us that you have run these tests on urine specimens from adults?

> Α. Yes.

All right. Those adults I take it had no history of renal failure or renal dysfunction?

> A. Yes.

All right. Those adults, as I understand it, had no cardiac problems. Do I have that correctly, they were healthy?

Yes, they were healthy adults.

All right. Were these adults 0. who were working in the Hospital?

> A. Yes, they were.

Q. Are these technicians in your lab?

A. Right, and myself and other

investigators.



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Q. All right. And how many individuals were involved in your sample group?

There are approximately 12, 13 A. individuals.

> All right. 0.

At the present time. A.

So, I take it then, Doctor, that you have taken a number of urine specimens from these individuals over the course of the last several months, have you?

> A. Right.

To run these tests?

Right. A.

And you have told, and I assume 0. of course that none of the members of the sample group have ever been on digoxin?

> A. Right.

Q. All right. Doctor, you have told us as well, or at least I understood you to say to Mr. Strathy yesterday that you have also run some of these water loading experiments in respect of blood specimens. Did I have that correctly?

> Yes, you do have that correctly. A.

Q. And were those blood specimens from the same individuals in the same sample group?





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A. Yes, they were.

Q. All right. And if I understood what you indicated to Mr. Strathy yesterday, the results of the assays run by these various techniques on the blood specimens did not indicate, or did not give you a reading which you could point to as being indicative of the presence of Substance X or the presence of digoxin. Do I have that correctly?

A. You have that correctly.

Q. But the urine specimens did.

A. They did, yes.

All right. So, when we talk then, Doctor, as Mr. Roland has discussed with you, about the merits of doing these tests on infant specimens.

A. Yes.

Q. I take it, and you have told us, that in order to do these tests on specimens of blood from infants, you would need first a very large amount of sample. Do I have that correctly?

A. Yes. I can't at this point tell you how large a sample I would need and I can't tell you what concentration I would require because I haven't done that work.

Q. All right.





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A.	So,	1t	would	have	to	be	Tooked	at.

All right, Doctor. But whatever the volume of the sample, do I take it from what you have said that in your mind you might require a larger sample than you would from an adult?

A. No, the size of the sample will be dependent on the concentration of Substance X in the sample.

All right. And that pertains 0. to blood specimens from infants?

> A. Right.

Right. Is there any reason Doctor why these tests could not have been done or could not now be done on urine specimens from infants known to have renal dysfunction? I take it you haven't done those tests?

- It could be, yes, it could be done. A.
- But they haven't been done?
- They haven't been, no.
- Q. All right. And similarly, Doctor,

I take it there would be no particular reason why you couldn't run these tests on urine specimens from children, infants with cardiac problems with some degree of renal dysfunction?

A. Could be done.



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That patient population clearly exists in the Hospital and it might be possible to do that?

> Right. A.

All right. And would there be any problem in doing that regarding the size of the sampling. Would you have any particular concerns?

> A. Well, not with the urine sample,

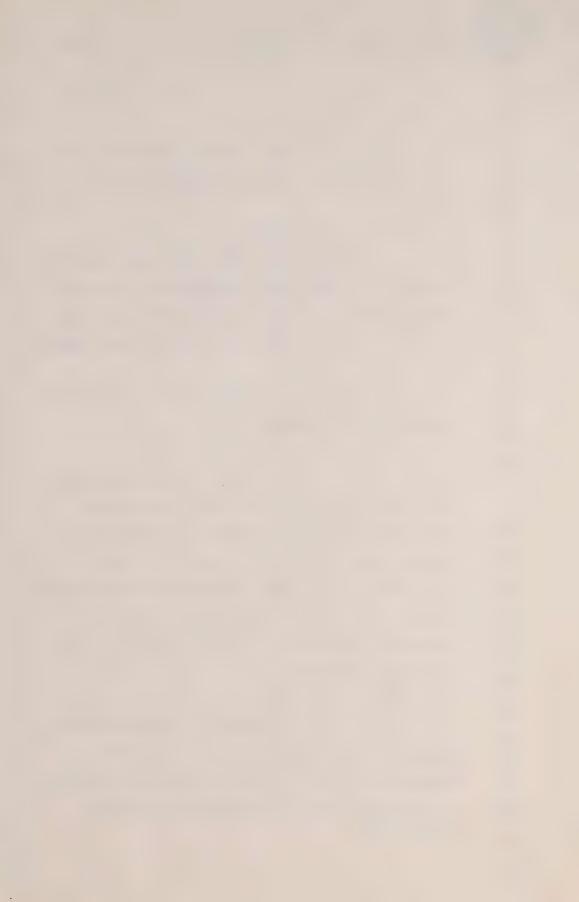
Q. All right. So, there is no deterrent in that regard?

> Α. No.

0. All right. Doctor, with respect to the results that you have thus far observed concerning these various tests, as I understood your responses both to Mr. Strathy and Mr. Roland, you have, on the basis of the urine specimens from these adults that you have tested, found an indication of the existence of Substance X in those specimens. Do I have that correctly?

> A. Yes.

All right. Is it Substance X alone, Doctor, or have you found as well other compounds that react in the same way or any similar way to digoxin, apart from what you are calling Substance X?



other fractions of the chromatogram, so, there may

purified one of these. The fraction which has the

maximum activity is by far the largest percentage of

well be more than one compound. We have only

A. We have found some activity in

And that is what you are calling

But you have seen, as a result

That's what I am currently

the activity.

Substance X?

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the purpose of the experiments to date as you have

or, I take it, any of these other like reacting

carried them out, together with your colleague, has been merely to identify whether or not Substance X

A. It has, yes. And you have told Mr. Roland that

of the assays on the urine specimens, you have also seen the apparent activity of other compounds that react like digoxin other than the one that you are

calling Substance X?

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calling Substance X, yes.

A. Yes.

Q. All right. The activity of those compounds has also been measured by you as a

result of these tests?



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substances are or are not present in the specimen.
Do I have that correct?

- A. That is correct, yes.
- Q. All right. So, I take it then, Doctor, that in all of the experiments that you have done since you commenced this research, you have not attempted, nor have you quantified or assessed the level or the amount of any of those substances that are present in the specimens. You didn't get an actual level?
- ${\tt A.}$ Well, we have quantified the dig.
 - Q. All right.
- A. And we followed these materials by quantifying digoxin activity. All the way through, the whole thing is extremely tight. In other words, I can say we lose 20 per cent when we do this run, we lose 20 per cent of the activity. Everything is quantified in terms of digoxinlike activity.
- Q. All right. And when you say that you got no reading or no result on the blood specimens that were tested, I take it then that you were unable to measure any digoxinlike activity on those specimens?
 - A. On the blood samples?



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Q. On the blood specimens?

A. In adults being water loaded,

Q. Yes, the ones you tested?

A. Yes.

Q. Yes, all right, Doctor.

Doctor, my questions with respect to the level or the quantification of your results flows from the fact that you referred Mr. Strathy, as I understood it, to the research that had been conducted by Dr. Valdes?

A. Yes.

Q. And we know that he tested results with known renal failure?

A. Yes.

Q. All right. And as I understand it, he also tested plasma or blood specimens of normal newborn infants not known to have been on digoxin?

A. Yes.

Q. Do I have that correctly?

A. Yes, I am sure you have.

Q. And we have seen, you will

recall when you last testified that we marked as an exhibit an article which you provided to us by Dr. Valdes which spoke about the results of the





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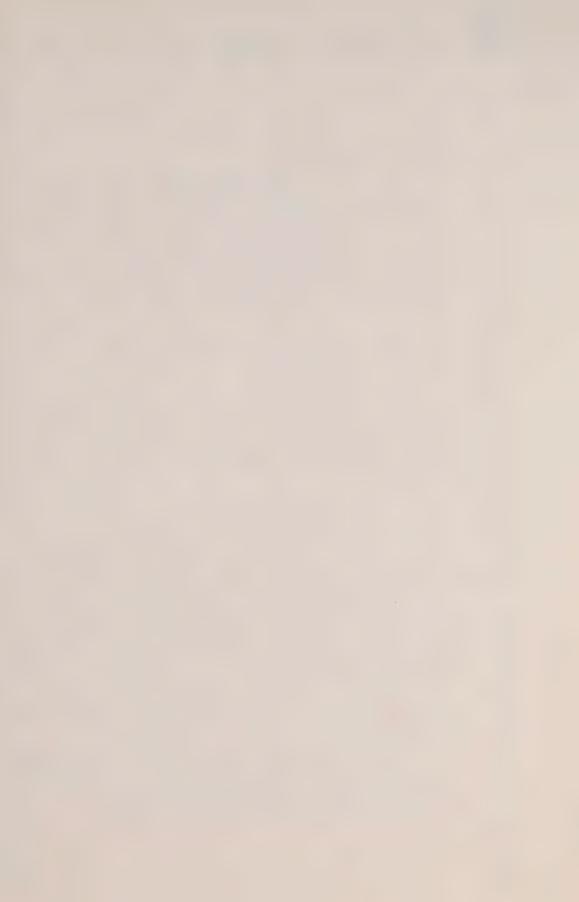
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research on the infants.

It is my understanding that as a result of those Valdes studies he found a substance in the blood of those adults that he tested and as well in the blood of those infants that he tested which reacted on assay like digoxin was expected to?

- A. Yes.
- Q. Do I have that correctly?
- A. Yes.
- Q. And in that sense his research was similar to that of Dr. Seccombe from whom we have heard who also tested neonates known not to have been on digoxin?
 - A. Right.
- Q. All right. And as I understand it, Doctor, the highest reading that Dr. Valdes found for this substance on either the tests that he did on the blood of adults or the tests that he did on blood of infants was 1.4 nanograms. Does that accord with your recollection?
- A. I can't recall but that might well be it.
- Q. Well, do you have any understanding as to what the highest recorded level was that Dr. Valdes observed as a result of his research?



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A. No, it was certainly under 4.
Q. All right. Doctor, with respect

Q. All right. Doctor, with respect to Dr. Seccombe of course we have heard his own evidence that the highest reading that he saw was 4.1 nanograms.

A. Okay.

Q. All right. And in asking you what the levels were that you obtained as a result of all your experiments to date, my purpose obviously was to put your results and your experiments in the context of those two other studies if it was possible to do so. And I take it that you do not have a quantification or a level, an actual level on any of the specimens that you have tested so far?

A. No. Well, if you are talking about the adult water load experiments?

Q. Those are the only onese you've done in that area, isn't it?

A. In this area - well, we have looked at a whole lot of premature neonates, as you know, and this was given in evidence before.

 $\ensuremath{\mathtt{Q}}.$ No, I am talking about the water loading experiments.

A. So, we had the digoxin measured in those samples. But in adults that are being given



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water loads, no, we haven't found any elevated serum concentrations.

Q. All right. And with respect to the urine specimens, Doctor, I take it you have been able to identify what appears to be Substance X, what you feel to be Substance X?

> Α. Yes.

As well, you have identified at least the presence of two other compounds that appear to have reacted in the same way as digoxin. Do I have that correctly?

A. Yes. There would appear to be two areas in the chromatogram that have digoxinlike activity apart from Substance X.

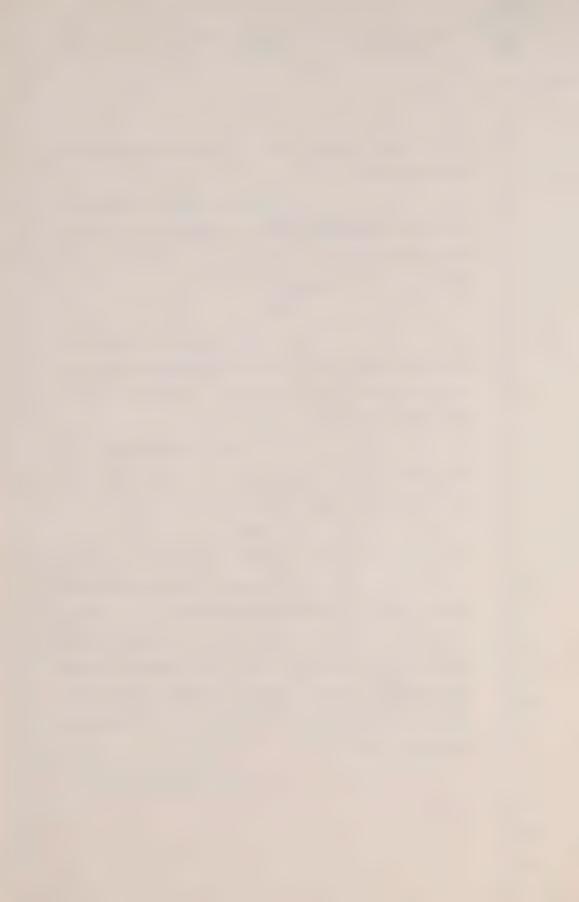
> Q. All right.

Or what we are calling Substance X.

Have you as well identified what appears to be a compound which appears to be reacting in a straight digoxin sense; in other words, have you had a specimen which you have tested since you have started this research that appears to contain both digoxin, Substance X and these other two compounds, or do you know?

I am sorry, I don't get that

question.



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that	you have i	dentified	substance	X and y	ou l	nave
also	identified	d activity	which app	pears to	be :	related
to a	compound o	ther than	substance	e X.		

Do I have that correctly so far?

- A. Yes.
- Q. Have you in any particular specimen found the combination of activity that Mr. Roland suggested as I understood him was possible, and that is the presence of digoxin in the urine specimen, the presence of substance X in the specimen and as well the presence of other compounds that react --
- A. No, we haven't because none of these people have been on digoxin.
 - Ω . That was my question.
 - A. None of these people have been.
 - Q. All right, thank you, Doctor.

Doctor, do you recall on the occasion of your previous testimony that you testified you had no personal experience as of that date in using the HPLC methodology for digoxin assays?

- A. That is right, yes.
- Q. You recall that?
- A. Yes.



- Q. That testimony was given on July 6th of this year?
 - A. Yes.
- Q. And as I understood your evidence and as I recall it you in fact said you had at that stage never used HPLC to test for digoxin.

 Do I have that correctly?
- A. We were about to commence at that time. I think your question came a day or two before we started our studies on HPLC of digoxin itself, yes.
- Ω . That was going to be my next question, Doctor.

Because you have now told us and indicated to Mr. Strathy yesterday and others have discussed it this morning that you have now developed the HPLC assays such that it is possible to run digoxin assays using that technique, and similarly if I understood your evidence yesterday, you have this combination of techniques, the HPLC and the mass spectrometry which is available for digoxin assay.

Do I have that right?

- A. We have developed a procedure by HPLC which separates digoxin from its metabolytes.
 - Q. Right. Isn't that the same



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thing, Doctor?

A. You might be calling it the If you are saying do I have an assay that I would in inverted commas market as an assay I would say no, I don't know, because an assay that is marketable is one in which one can quantify the results of digoxin in an unknown sample.

> 0. I understand.

And at the present time our method has been more how do we separate digoxin from its metabolytes; how do we separate it from substance X, and can we identify these compounds and do they have very different mass spectra, so this has all been looked at.

Doctor, I take it then when you testified last on July 6th before the Commission you did not then have in the Hosiptal to your knowledge an adaptation, if you will, of the HPLC method which permitted digoxin assays to be performed; nor do you today in the sense of a system that will provide you with a quantitative result.

Do I have that correctly?

I wouldn't provide a quantitative result today, yes, on a sample for digoxin using HPLC.

Ω. And if I understood what you



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told the Commissioner you think that that could be worked up in relatively short order?

- A. Yes.
- Ω . But as the matter stands today you couldn't get it to corroborate the result?
- A. Right now I couldn't. You are quite correct.
- Q. So when you said yesterday that you developed an HPLC and mass spectrometry method for the measurement of digoxin you meant that you have developed a technique that will show you definitively whether or not digoxin is present in the specimen that is submitted to that analysis but not the amount of digoxin.
 - A. At that point in time, yes.
 - $\Omega.$ All right. Doctor, I'm just trying to understand the methodology.
 - A. Right.
 - Q. And what has happened, and what is the case today as opposed to what the state of affairs was in July.
 - A. Yes. Right.
 - Ω . In respect to the HPLC method that was available in the Hospital then, what have you had to do to adapt it to permit you to now



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identify the presence of digoxin in any given specimen? What did you have to do that wasn't the case in July?

A. We haven't used it essentially - sorry.

THE COMMISSIONER: Just a moment.

MR. ROLAND: Just one interjection here. I don't want to let the examination go too far along so that I am out of the chronology of things but Miss Cronk is asking about his experience with HPLC in digoxin testing, and he indicated, the witness indicated that he didn't have any at the time he testified in July and that he began doing these tests a few days later.

I am afraid at least with me and perhaps a few others Miss Cronk left the impression he didn't have any experience with HPLC, and that of course --

MS. CRONK: I said for digoxin.

MR. ROLAND: In his testimony and both in his curriculum vitae when he was introduced the last time he has a great deal of expertise with HPLC.

MS. CRONK: I am sorry. My question specifically was for digoxin assays.



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I knew that, Doctor, and I was not intending to suggest otherwise.

MR. ROLAND: It sounded to me that Miss Cronk was suggesting she was launching into new frontiers.

MS. CRONK: Well, I thought he was doing that but maybe not in the way you suggested.

Ω. Doctor, my question to you and perhaps I have misconceived of the situation, is that HPLC technique in July of this year was not used for digoxin assays in the Hospital and accordingly for that particular purpose you had no experience with that technique for digoxin assay. That I have correctly, do I not?

A. Yes.

Q. We now know that you are using the HPLC technique as part of these experiments to isolate and identify the presence of digoxin in any given substance?

A. Yes.

Q. Was the technique capable of doing that in July?

A. Easily.

Q. All right. So it is not then, as I was about to ask you, a situation where you had



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to adapt the technique or modify it in any way to make that determination on HPLC? That could have been done in July of this year?

A. Right. And July of the previous year as well.

Q. I take it then, Doctor, as part of the research which you have undertaken and which is continuing, you are now simply looking to that technique as a procedure to assist you in identifying the presence of digoxin, but no technical variation on what existed in the Hospital as a HPLC technique in July has happened? There has been no change in the technique?

A. Well, we hadn't measured digoxin in July, but the technique is basically HPLC of which I have had a lot of experience.

Q. All right. And there was nothing specifically that you had to do either with the equipment available in the Hospital or the methodology with which you were previously familiar to accommodate that technique to run these tests to identify the presence of digoxin?

A. No. I just had to I guess tap my years of experience in HPLC.

Q. Yes, I understand.



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Doctor, we have heard and I don't intend to dwell at length on it but we have heard a number of comments this morning concerning the nature of discussion that took place at a meeting at which you attended prior to giving your evidence here.

Do you recall attending a meeting on October 7th at which Mr. Roland, Counsel for the Hospital was present and I was present?

A. Yes, I do.

Doctor, you have heard me say this morning that it was my understanding as a result of those discussions that you did not then feel yourself to be in a position to discuss the results of the water loading experiment that you had undertaken by virtue of the fact that the results were preliminary and that you were not yet in a position to speak with any confidence as to their validity or their meaning.

That has now happened, Doctor, in the sense that you have now given evidence with respect to those experiments, and I would ask you since the date of October 7th when that meeting took place and yesterday, was there anything further that happened in your research or any results that came to your

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attention from those experiments which led you to give that evidence yesterday when you previously felt it was premature to discuss the testing at all?

A. Well, there were certain

aspects on October 7th that were very hard scientific data as far as I was concerned and there were other areas that I was awaiting data and results, and some results have obviously come in, so that I am confident that we have developed procedures to isolate a compound - you can call it substance X - and not only developed procedures to purify that compound but we have developed procedures to obtain a lot of information as to what that compound actually is.

Ω. Doctor, my question to you essentially is are you more confident today as to the reliability of these experimental results than you were 10 days ago?

A. Well, I have more knowledge today than I had 10 days ago. That is all - you know, the data that we had 10 days ago hasn't changed. We have added to it.

Q. When you say you have added to it and you have more knowledge I take it you have run more assays?



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- A. Yes, especially the mass spec.
- Ω_{ullet} Had you 10 days ago run any assays and obtained any results on your mass spec from your colleague at the Best Institute?
- A. We had data on digoxin and we had data on these metabolytes but we didn't have data on substance X.
- Q. I take it then sitting here today, Doctor, you are confident on the basis of the experiments that you have conducted to date you have successfully been able to identify substance X by the techniques that you have described in the urine specimens of this sample population?

Are you prepared to --

A. When you say "identify", if you mean I can put a molecular structure to it I will still hesitate to do that.

If you say identify - have we purified it, yes, we have purified it. We have a lot about its molecular weight, about its probable structure and we may even venture some suggestions as to its actual structure.

- Ω . All of that I take it, Doctor, was well underway and was the case 10 days ago?
 - A. Except that we didn't have the



mass spectra 10 days ago.

All right. 0.

Yes, the experiments leading to that had been underway for three months. But the mass spectra only became available about 9, 10 days ago.

I see, Doctor. So that all of 0. the assays that have been run by your colleagues at the Best Institute on mass spectrometry have been undertaken within the last 10 days? Do I have that correctly?

Α. No. All the studies on substance X, yes.

Q. I'm sorry, Doctor, I thought that is what we were talking about.

A. He had measured digoxin, looked at the digoxin spectra, the digoxin metabolytes, looked at their spectra.

> I see. 0.

A. And this all occurred and when these compounds were run by us, the digoxin and metabolytes were run by HPLC you have a separated separated fractions were given to Dr. Kuksis who then ran mass spectra on them.

> 0. I take it then --

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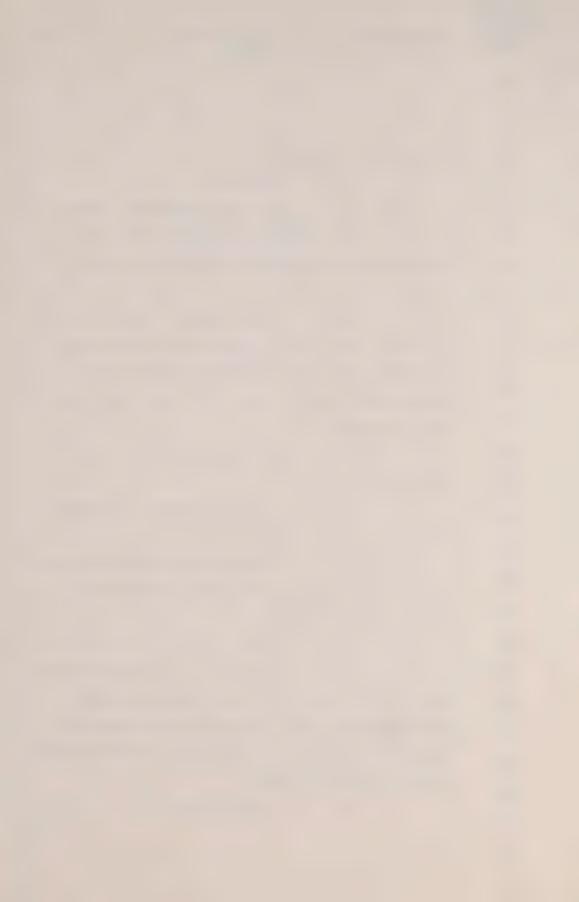
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	Α.		We	then	compared	that v	vith	1	
substance	X	but	that	was	only	obtained	about	10	days
ago.									

- Q. I take it then, Doctor, so that I am very clear that I understand, all of the tests that have been run regarding this substance X as distinct from digoxin and mass spectrometry have been undertaken and the results have come back from the last 10 days?
- A. All of the mass spectra data, yes.
- O. All right. And it is on the basis of that additional knowledge and that additional information that you today can say with confidence that the technique and the experiments which you have undertaken permit you to identify with certainty substance X in any given urine specimen of your sample population? Is that --
- A. It has certainly helped largely to build my confidence in our data, yes.
- Q. Doctor, now other than those tests and those assays that were run in the Institute, has there been any additional or different tests undertaken in the last 10 days as part of these water loading experiments?



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tests.

A. Yes, there have been lots of

THE COMMISSIONER: I'm sorry, what was that?

THE WITNESS: Additional tests that have been undertaken.

MS. CRONK: Ω . And are they simply more, Doctor, of the same assays from urine specimens that you previously conducted? More in number?

A. I would rather not get into it if that is possible, but we have done a lot of additional studies.

Perhaps I could add one thing that if you do water loading experiments of this type you can isolate by HPLC fractions that have digoxin activity as we know. We call that substance X perhaps Y and Z.

You can also isolate fractions which have activity in other assays, immunoassays. Not digoxin immunoassays, and so we have done a lot of work on the other immunoassays as well.

Q. Doctor, within the last 10 days have you undertaken any further tests as part of these experiments on blood specimens from the same adult sample population?



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No. Α.

So you have not? 0.

A. No.

So they had all been done as Q. of 10 days ago?

> Yes. Α.

Within the last 10 days have 0. you undertaken any assay tests or experiments on any urine specimens from any infants at all?

> Α. No.

All right. Then within the 0. last 10 days have you undertaken any assays or tests on plasma specimens from infants at all?

A. No. I am sure - we always have been doing digoxin assays --

> 0. As part of this water loading --

As part of the study, no. A.

All right. 0.

Α. We have not subjected any patient population to the water loading study.

Doctor, may I turn then Ω . briefly to another area?

You told Mr. Strathy to the best of your recollection - this is in the context of the death of Allana Miller and digoxin assays that had



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been run in respect to that child - that another sample of the oral medication or elixir from Ward 4A/B had been tested you thought on Thursday?

- A. Yes.
- Q. Do you recall that?
- A. Yes.
- Q. You were talking about

Thursday, March 19th, or the following Thursday, March 26th, 1981?

A. No, I thought it was the 19th.

MS. CRONK: Mr. Registrar, would you show the Doctor, if you would, please, Exhibit 32B?

Q. Doctor, I would ask you to turn if you would to Tab 45, page 27, please.

Do you have that, Doctor?

- A. Yes.
- Q. Doctor, at that page, on page, the bottom half of page 26 and the beginning of page 27 we see the results of the various digoxin assays that were carried out on March 19th.



Soldin re.dr. (Cronk)

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Q. Can you help me, doctor, as I understood it, you thought the assays were conducted on that sample of elixir on that day. Are there any results set out there on March 19th that pertain to that assay test?

A. Yes, there is, on the 18th of March. I'm sorry, it was the 18th of March.

 Ω . And, doctor, when you are looking at the entries for the 18th of March, are you referring to Items 12 through 14?

A. Right, to 15.

Q. I'm sorry, through to 15.

A. Right.

 Ω_{\bullet} And, doctor, as I read the entries then, a sample of lanoxin or the oral elixir was assayed at least four times on that day.

A. Yes.

Q. And you were aware of that, doctor, I take it at the time, the weekend of March 21st when you were called in to supervise the assays on Allana Miller and, subsequently, on Justin Cook?

A. Yes, I was.

Q. What was your understanding, doctor, as to why tests were being undertaken two days previously on a sample of oral elixir from this



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A.	Wei	ll, I thi	nk I i	.ntimated
that we had a meeting	in Dr. H	Hill's of	fice,	and Dr.
Hill indicated to me	that then	re was so	me con	cern
on 4A/B about digoxin	. This	is the f	irst I	had
heard of any concerns	personal	lly as to	probl	ems
on 4A/B and digoxin.	Не ехрі	ressed, 1	think	, if I
recall rightly, that	the conce	erns may	be att	ributed
to the pharmaceutical	prepara	cion. I,	in di	scussion
with him since,I went	to Ward	4A/B and	l got a	sample
of digoxin from that	ward and	gave it	to Dr.	Ellis,
apparently.				

Q. For testing?

A. For testing, yes.

Q. And do you see here,

doctor, beside those various entries of March 18, the results of four assays that were conducted on that sample?

A. Right.

Q. Was it one sample or more

than one?

A. No, it was one bottle.

Q. Can you help us, doctor,

as to what the significance, if any, is as to the results that are recorded?



be, essentially.

Soldin re.dr. (Cronk)

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A. They are as they should

Q. I take it, then, that on the basis of that test, there was nothing to indicate that the preparation of the elixir had contained a high concentration of digoxin than had been indicated by the manufacturer?

A. Right.

Q. And we know, doctor, that when it came to the tests which were done on the 21st of March, you repeated a like test on another sample of oral elixir from the ward and obtained a like result.

A. Correct.

MS. CRONK: Mr. Commissioner, I will only be a few more minutes. I think I can finish by quarter after one.

THE COMMISSIONER: What do you have planned for us for this afternoon?

MS. CRONK: The next witness is Mr. Cimbura, sir, and he is not available until tomorrow morning, so we are looking at a short afternoon.

THE COMMISSIONER: I think, put to a vote, that everyone would be in favour of your



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completing in fifteen minutes.

MS. CRONK: I would have thought so.

THE COMMISSIONER: If that is

possible. Perhaps Dr. Soldin could lead the cheering section!

MR. ROLAND: I think Dr. Soldin is anxious to get back to his experiments!

MS. CRONK: I can understand that.

Q. Doctor, other than the tests of the oral elixir that were conducted on March 18th and the assays that were conducted on the 21st of March, are you aware of any other assays for digoxin conducted in respect of the preparations of digoxin available on that ward during this week, other than those two?

A. No, I am not aware of any others.

Q. To the best of your knowledge, then, doctor, I take it no assays were conducted in respect of digoxin ampoules that were available on the ward?

A. That is correct.

Q. Doctor, you will recall as well this morning, I believe it was Mr. Hunt, during the discussion with him, he drew your attention



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to the previous evidence of Dr. Costigan --

Α. Yes.

-- regarding the time at 0. which Dr. Costigan, as he recalls it, was informed of the death of Allana Miller and his activities early that Saturday morning.

> Α. Yes.

0. As I understand your evidence, to the best of your recollection, it was your belief at the time that you testified yesterday that you were alerted to the death or the arrest of that child by Dr. Costigan by virtue of the telephone call at two or three in the morning, during the early hours of March 21st?

> Α. Yes.

Is that correct? 0.

Α. Yes.

Q. And in that regard, we have heard that your recollection and Dr. Costigan's differ?

> Right. Α.

0. You told me yesterday,

however, that, in respect of the telephone discussion that you had, you thought with Dr. Costigan, the decision was made at that time to run digoxin assays

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in respect of a sample of the oral medication from the ward. You also told me that you then, after having received the telephone call from, you thought, Dr. Costigan, called Candy Cheong and instructed her as to how to run the assays?

- A. Right.
- Q. Do you recall that?
- A. Yes.
- Q. As I understood your evidence, doctor, you instructed her to run the assays at various dilutions and, as well, to run an assay on the second sample of oral elixir from

A. Yes.

- Q. Do I have that correctly?
- A. Correct.
- Q. Do I take it then, doctor,

that whichever doctor it was that you spoke to at two or three in the morning, the matter of running the assays on the Allana Miller sample at a number of dilutions was a matter specifically discussed then between you?

A. Well, it was discussed between me and the doctor but, whether it was discussed at three in the morning or whether it was



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discussed in another conversation later in the morning, I can't tell you. Certainly, we got samples for analysis prior to Candy Cheong doing

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Wards 4A/4B?

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the entire run.

And do I take it correctly, 0. doctor, do I have it correctly, that the purpose of running the assay at various dilutions, or at least the fact of doing that, was motivated by the concern that there might be a high level, there might be a problem with this level?

> Α. Right.

Was that related, doctor, 0. to your discussion the previous week, which you have now told us about, in which it was indicated to you there might be a problem with digoxin on

> Yes, I'm sure it was. A.

0. And similarly, with

respect to the assay which you instructed Miss Cheong to perform on the sample of oral elixir from the ward, did you have in mind, when you ordered that, the fact there had been a test done earlier in the week on another sample of elixir?

> Α. I knew there had been, yes.

And why, in those 0.



circumstances, doctor, were you ordering another assay to be done on another sample from the ward of elixir?

A. Well, in the event that the drug had been administered from this particular bottle and I wanted to know what the concentration of digoxin was in the bottle.

Q. Dealing as well generally with the issue of readings that you have . done of concentrations of digoxin that you have seen since the end of March 1981. As I understood your evidence with Mr. Strathy early this morning, you indicated that you thought, since July of 1981, when you became involved in conducting the various digoxin assays in the Hospital, that you had seen, you thought, about three cases where the levels were greater than 50 nanograms; do I have that correctly?

- A. Possibly, three.
- Q. Possibly, three. You

were approximating three?

THE COMMISSIONER: Greater than

what?

MS. CRONK: Greater than 50 nano-

grams.



A. In other words, gross contamination.

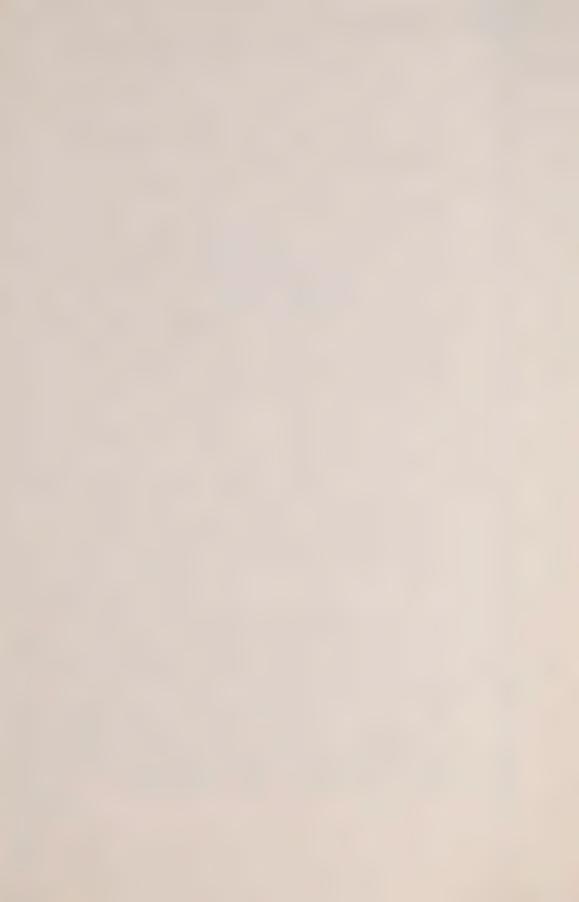
Q. Doctor, that is the issue I would like to explore with you. As I understood it, you suggested that levels of that kind could have occurred because of contamination by one of two possible methods. The first was that a syringe was used to administer digoxin and then the same syringe was used to draw a blood specimen which was then assayed for digoxin.

- A. Right.
- Q. Amongst other things?
- A. Yes.
- Q. Was that, in fact, doctor,

to the best of your recollection, the explanation that applied to those particular readings that were greater than 50?

A. No. I think the explanation was the second one, which was that digoxin had been administered via an IV line and that a sample was then drawn for digoxin assay out of the same line shortly thereafter.

Q. And in the cases in which you recall a level of greater than 50, they were explained by virtue of that circumstance?



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A. Yes. There was no clinical symptomotology associated with that level.

Q. As I understood it, you told Mr. Hunt this morning, leaving aside those cases of the kind of contamination that you have discussed where the levels were greater than 50, the highest level, or the highest reading on digoxin that you have seen since July of 1981 is under 20 nanograms; do I have that correctly?

A. Except for Murphy, possibly, yes. No, Murphy was around 25.

Q. Is it the Gary Murphy case that you are recalling when you say you had seen a level under 20, doctor? Is that the one that comes to mind when you think of high levels since July of 1981?

A. Yes.

Q. With the exception of Gary Murphy, have you, since becoming involved with the digoxin assays at the Hospital, seen any other levels between 15 and 20 nanograms, other than Gary Murphy?

A. I think we had possibly one, at around 15, a few months back, three or four months back.



Soldin re.dr. (Cronk)

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Q. Was that matter investigated and enquiries made?

- A. Yes, it was. Yes.
- Q. What was the explanation

for that level, if any?

A. That the patient had taken an overdose of digoxin. Actually, it was a young kid who had swallowed a lot of tablets.

Q. Not an infant in the

Hospital?

- A. No, not an infant.
- Q. Someone who was admitted

for the reason of an overdose?

- A. Yes, and now is well. Yes.
- Q. Doctor, as I understand

it, again, this was a matter discussed in part earlier this morning, that one of the possibilities that you are currently examining as part of your ongoing research is whether there may be clinical conditions or events which occur during resuscitation efforts that may trigger the release of substantial or significant quantities of Substance X; do I have that correctly?

- A. Yes.
- Q. And in your discussion

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yesterday with the Commissioner and the request that you made for receipt of various tissue samples, do you recall that, for testing purposes, I take it you had in mind at the time you were talking about that request the research that you have been conducting to date concerning the possible effect of resuscitative efforts as well?

A. Right.

Q. Doctor, as was reviewed this morning, since March of 1981, we have heard in evidence that the Hospital has done digoxin assays on post mortem blood samples on virtually all children, as you described it, who died since March 1981 on Wards 4A/4B?

A. Yes.

Q. Is that correct?

A. Yes, you have that

correct.

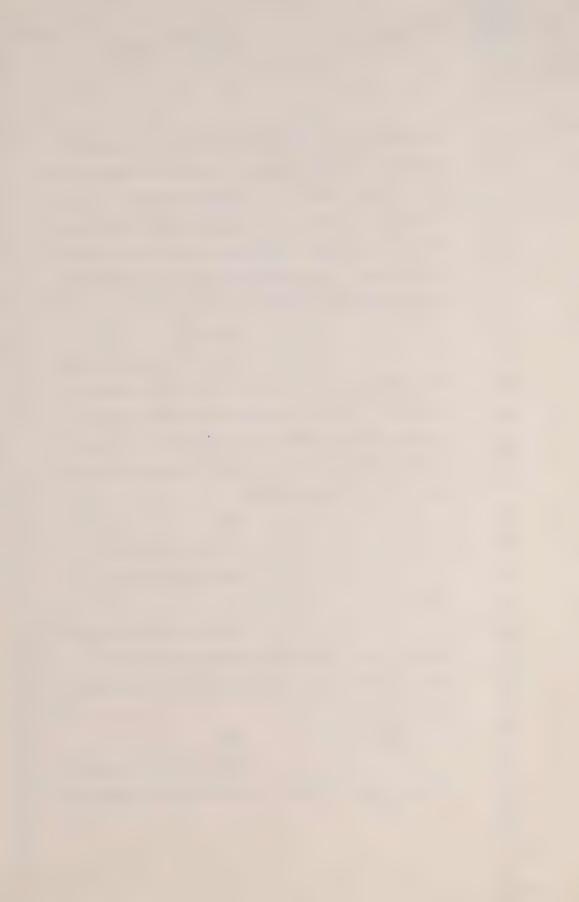
on digoxin?

Q. And you told Mr. Hunt,
I'm sorry, Mr. Young, this morning that many of
those children were children who would have been

A. Yes.

Q. You told Mr. Young as

well that many of those children are children who





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would have been the victims of unsuccessful resuscitation efforts; do I have that correctly?

A. I don't know how many.

Some would have been.

Q. Some would have been?

A. Yes.

Q. I suggest to you as well that there is a great likelihood that some of those children might as well have been in renal failure, do you agree with that, at the time of their deaths, in all of those deaths since March 1981?

A. Some may have, yes.

Q. And, as well, some of those children would not have been on digoxin therapy at the time of their deaths; there is a likelihood that is true?

A. Yes.

Q. I suggest to you as well that some of those children may well have experienced defibrillation as part of the resuscitation efforts that were undertaken?

A. Right.

Q. Do I have that correctly?

A. Yes.

Q. As you told Mr. Young, and



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as I discussed a few moments ago, leaving aside the three cases where contamination of samples resulted in levels of greater than 50 nanograms, the highest digoxin reading of which you are aware since July of 1981 is in the case of Gary Murphy?

A. Yes.

Q. Doctor, I suggest to you that, since the end of March 1981, no child has died on Wards 4A/4B exhibiting quite the same and precise measure of clinical conditions, renal dysfunction and resuscitative insult to generate levels as high as those which you recorded on March 21, 1981 in respect of Allana Miller and as high as the ones that you recorded in respect of Justin Cook on March 22nd? That is the situation, is it not, doctor?

A. Yes.

Q. And that is true even though the technique available in the Hospital for the testing of digoxin and for the running of digoxin assays since that time has been an RIA methodology, which, in your view, is not sufficient to segregate out substance X; is that correct?

A. Right.

Q. Doctor, with respect to



the question of the provision of tissue samples, I would just like to be clear about one other matter.

If it should be the case that there are specimens that still exist today and may then, therefore, be available for further testing for digoxin, would you be concerned, as a biochemist who might be involved in the conduct of those assays, as to their stability, given that those specimens would be at least two and-one-half years old? Would that present any concern to you?

A. That would present a concern. It depends on how they have been stored. That would be quite a crucial issue.

Q. Doctor, do you, in fact, know how the specimens that were once at the Hospital and which left the Hospital during that first week after these deaths, the end of March 1981, have been stored since that time?

A. No, I don't know.

Q. Do you have any parti-

culars on that at all?

A. No.

Q. Can you help me then,

doctor, with what you meant when you suggested there had been a lack of care taken in the storage of those



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had been stored.

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A. No, I didn't suggest that.

Q. I thought, this morning,

you said --

MR. ROLAND: That wasn't a suggestion. This is the first we have heard that.

THE COMMISSIONER: I thought there was something he indicated that someone, somehow, had not looked after the samples, except they are in storage.

THE WITNESS: My inference, if you will allow me to repeat it, is that I have -- well, prior to this, my evidence today, I have been somewhat critical of the analytical procedures employed, and all I did was --

 $\text{MS. CRONK: } \ \, \Omega. \quad \text{Is that what you}$ were referring to, doctor?

A. Right.

Q. And you were not referring to the fact that there may have been some deficiency, as you understood it, in the way any of these specimens may have been stored?

A. I didn't know how they

Q. I wouldn't have thought so,





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doctor.

Finally, doctor, as I understood your evidence this morning, you indicated that you were involved in the conduct and performance of digoxin assays with respect to Gary Murphy; do I have that correct?

A. Yes.

MS. CRONK: Mr. Registrar, could you serve the doctor, if you would, please, Exhibit 172.

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Q. Doctor, would you turn to page 141 if you would. This exhibit is a copy of a part of the medical record of Gary Murphy, that part which applies to the time period immediately before and at the time of his death.

A. Yes.

Q. Do you have page 141, Doctor?

A. Right.

Q. Right. Doctor, we have heard in evidence previously that the last antemortem digoxin level which was taken in respect of Gary Murphy was taken on April 4, 1983?

A. Yes.

Q. And that no levels were taken thereafter until the date of his death on April 23rd. We see on page 141 Sample No. 212099.

A. Yes.

Q. Which appears to have been taken at 4:30 a.m. on April 24th.

A. Yes.

Q. The child died on April 23rd at 6:37 p.m. in the evening. May I ask you, Doctor, did you personally conduct or supervise the digoxin assays that were conducted in respect of that sample?

A. I supervised them, yes.

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Q. All right. I appreciate, ou do not have any digoxin book ma

Doctor, that you do not have any digoxin book materials available to you in this form with respect to assays conducted in April of this year, but can you help us now as to the number of dilutions that were involved with respect to this sample which ultimately yielded a level of 18.7 nanograms. Do you have that information with you today, Doctor?

A. Yes, I am just reviewing it.

It was done times 5, times 10, times 20.

Q. It was done neat?

A. It was done straight times

Q. And was the result when it was done neat greater than 5?

A. Yes, it was.

Q. And the results when it was

done times 5 dilution was what?

A. Was 21.

Q. And the result when it was

done times 10?

5 times 10 times 20.

A. It was 24.

Q. And times 20?

A. 24.

Q. And those of course we know



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are measurements in nanomoles per litre?

Q. And when the 24 nanomoles level is converted, that results in 18.7 nanograms, as indicated on page 141?

Yes.

A. Yes.

Q. All right. Doctor, there is an indication on this form of therapeutic drug monitoring cumulative report that the specimen involved was a plasma specimen. Does the information available to you there indicate the circumstances under which that sample was taken?

A. Well, not in this sheet here but in my notes here I do have - yes, this was a sagittal sinus sample. 212099 was a sagittal sinus sample.

Q. And do you know, the sample was obviously taken many hours after the child's death because Gary Murphy died at approximately 6:37 p.m. on the evening of April the 23rd. Was this sample taken during the course of an autopsy, do you know?

A. It must have been, yes.

Q. Well, do you know whether

it was?

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It must have been. Α.

> Q. Because if not we can find that out from others, Doctor?

> > Α. It must have.

Q. All right. I question that Doctor, only because the sample time appears to be 4:30 in the morning.

Yes.

0. That would suggest to me that it may not have been taken at autopsy. Doctor, would you turn as well if you would please to page 147 of the Murphy chart. We see there as well, Doctor, a number of other samples with the digoxin level results being reported. I would refer you first to the sample referred to in the first column, Sample No. 212425 which appears to have been taken at 11:00 p.m. on April 23rd. Do you see that, Doctor?

> Α. Yes.

All right. That appears to 0. be a plasma sample?

> Α. Yes.

0. All right. Doctor, once again, did you either conduct or supervise the performance of the assays conducted on this sample?

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2	A. I did, yes.	
3	Q. All right. Can you help m	ie
4	as to what the dilutions were to arrive at that	
5	result? Was the sample done neat?	
1	A. Yes, it was done the same	
6	dilutions neat times 5 times 10 times 20.	
7	Q. All right. And what was t	he
8	results when it was done neat, was it simply off	the
9	maximum?	
10	A. Yes, it was.	
11	Q. And when it was done at a	
12	dilution of 5?	
	A. It was 24.5.	
13	Q 24.5?	
14	A. Yes.	
15	Q. And when it was done times	
16	10?	
17	A. 24.	
18	Q. And when it was done - was	
19	it then done times 15 or times 20?	
1	A. Times 20.	
20	Q. And what was the result	
21	times 20?	
22	A. 22.	
23	Q. 22?	
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A. Right.

All right. I take it then, Q. Doctor, that when a result of 24 nanomoles is reported, that was the number selected as the result of a dilution of times 10 and that was reported?

> Right. A.

And that reading is identical 0. when converted to the reading of 18.7 nanograms?

> Α. Yes.

Q. Doctor, there is a footnote which appears below the level of this sample which indicates that the specimen was that of heart blood. Do you see that?

> A. . . Right.

0. Does that accord with your

Α. It does, yes.

Doctor, do you have any Q. information or knowledge as to the circumstances under which that sample was taken?

> Yes, I do. Α.

0. All right. To the best of your knowledge, when was the sample taken. It is 11 o'clock at night, and the child died at 6:37 p.m. earlier that evening. Do you know whether or not an



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autopsy was commenced that evening?

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A. I think the sample was taken - it might have occurred - my understanding is that

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that sample was not taken at autopsy.

6

Q. All right. Do you know who took the sample, Doctor?

7

Α.

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Q. I am sorry, I didn't hear you,

I think it was a heart puncture.

9

a heart puncture?

on the RIA method.

this year?

10

A. Right. Well, it was Dr.

11

Cloutier who brought the sample to Joan Hayes who performed the analysis.

12

Q. Is Miss Hayes in your lab?

13

A. · · Yes.

14

Q. Were the assays conducted on

15

these two samples that we have just looked at,

16

Doctor, conducted on the FPIA method or the RIA method?

17

A. They were conducted on the

18

FPIA method -- sorry, sorry, sorry. These are all

19

Q. Were they as well tested on

20

the FPIA method which we know was introduced on

21

an experimental basis in the hospital in April of

22

A. Yes, they were.

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Q. All right. Doctor, let's deal with the one that we have just looked at, Sample No. 212425. What was the result when that sample was assayed on the FPIA method?

A. 24.6.

Measured in nanomoles? Q.

Λ. In nanograms per litre. I

have converted it. It was 31.5 nanomoles.

0. I am sorry, Doctor, what was it in nanomoles?

> Α. 31.5.

0. And it was 24.6 nanograms?

Nanograms per litre, yes. A.

0. So, it was a higher reading then that had resulted on the RIA for the same

> A. Correct, yes.

Q. All right. And how many times

was the sample diluted for the FPIA method?

THE COMMISSIONER: We will be looking

at what page?

sample?

THE WITNESS: It was diluted five fold.

MS. CRONK: Q. Mr. Commissioner, we

are at page 147.

THE COMMISSIONER: Oh, yes, all right.



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Soldin, re.dr. (Cronk)

1	1	
2	2 MS. CRONK: I am still look	ing at
3	the first sample.	
4	4 Q. Was it run then fir	rst neat,
5	5 Doctor?	
6	A. That particular sam	mple I don'
7	see a recording of it being run neat, no.	
	Q. What was the first	dilution
8	at which it was run?	
9	A. It was times 5.	
10	Q. And what was the re	sult?
11	A. 24.6 nanograms per	millilitre
12	Q. And was it then dil	luted times
13	13 10?	
14	A. No, it was run once	by FPI -
15	it was run four times by RIA.	
	Q. Oh, I see, Doctor,	I am sorry
16	So, it was run once on FPIA and the result	was 24.6
17	nanograms?	
18	A. Right.	
19	Q. May we turn then ba	ack, Doctor
20	if we would just for a moment to page 141,	, the sampl
21	that we looked at a moment ago.	
22	A. Yes.	
23	Q. We know that the re	sult on

the assay reflected on this page was 24 nanomoles or



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Soldin, re.dr. (Cronk)

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2	18.7 nanograms and you have told me the various
3	dilutions that were undertaken?
4	A. Yes.
5	Q. I take it that that result
6	and all of those dilutions pertain to the running
7	of an assay on the RIA technique on that specimen?
	A. That is correct, yes.
81	Q. Was this specimen also tested
9	on the FPIA technique?
10	A. Yes, it was, both of those
11	were.
12	Q. All right. And was the sampl
13	run neat on the FPIA?
1	A. It was run with a tenfold
14	dilution.
15	Q. I am sorry, Doctor, just so
16	I am clear. It is Sample No. 212099?
17	A. Yes.
18	Q. All right. Was it run neat
19	first?
20	A. It was run neat first and
	then times 10.
21	Q. All right. What was the
22	result when it was run neat?
23	A. It was above the highest
24	



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1 standard, so, that was 6.4. 2 0. The highest standard was 6.4 3 nanomoles? 4 Yes, nanomoles. A. 5 Does that convert to 5 nanograms? 0. 6 Α. Right. 7 All right. And what was the Q. ' 8 result times a dilution of 10? 9 Α. 29.3. Q. 29.3. nanomoles or nanograms? 10 A. Nanograms per millilitre. 11 What was it in nanomoles, 0. 12 Doctor? 13 A. . . 37.5. 14 I take it then, Doctor, in 15 respect of both of those samples, the results on the FPIA resulted in higher readings? 16 A. That's correct. 17 0. Than did the RIA? 18 A. Yes. 19 Q. All right. Were the results 20 obtained on the FPIA testing mechanism reported as 21 well, do you know? 22 No, just the RIA method. 23 0. Was there any reason for that,



1	
2	Doctor?
3	A. Well, at that point in time
4	we were not reporting the FPIA results.
5	Q. Did that have some relation-
6	ship to the fact that it was a newly introduced
	mechanism to the Hospital?
7	A. It wasn't yet officially
8	introduced into the Hospital.
9	Q. This is the end of April,
10	1983?
11	A. That's right.
12	Q. When was it officially
12	introduced. I thought it had been that month?
13	A No, about then, but it wasn't
14	introduced on the night of the Murphy death.
15	Q. Finally, Doctor, back to
16	page 147 if you would, please.
17	A. Yes.
18	Q. Do you have that?
19	A. Yes.
33	Q. The last sample, Doctor, which
20	we haven't looked at is the one reported in the
21	third column over. It is Sample No. 212098.
22	A. Yes.
23	Q. Taken at 1845 hours on April



24th?

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A. Yes.

Q. Do you see that, Doctor?

Α. Yes.

The level reported there is 0.

greater than 6.4. I take that to be in nanomoles?

> A. Nanomoles, yes.

0. All right. And if we look to footnote C which is highlighted Doctor, we see that that is a specimen of heart blood?

> Α. Right.

All right. And we see as well a reference to a footnote labelled C-2 analysis performed on TDX instruments. Does that mean that this sample was assayed on the FPIA methodology?

A. Yes.

All right. Was it as well assayed on the RIA methodology?

> No, it wasn't. A.

Was there any reason for 0.

that?

A volume problem, there wasn't Α.

enough sample.

0. To do it on the RIA?

A. Both ways, yes.

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Q. All right. So that when we seen then the reading of greater than 6.4, was that the result of a neat assay of this specimen on FPIA?

> Yes, it was. Α.

0. All right. And if we turn over, Doctor, to the very next page it appears to be the same sample number and the result this time shows a reading of 25 nanomoles?

Yes, that's right.

0. Was that the end reading on the FPIA assays conducted on this specimen. Was that the final reading, Doctor?

No, my recollection is that Α. we only did it once on the FPIA.

The report at page 148 appears to apply to the same specimen number taken on April 24th, 1983 but you will note that the timing of this specimen is different?

Yes. There was a problem. What occurred was that a second sample was brought down by Dr. Cloutier to Joan Hayes. So, on the first sample she only did an FPIA sample which she got a result of 6.4 for.

> Of greater than 6.4? Q.

Greater than 6.4. A.



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2	Q. Greater than 5?	
3	A. Right.	
4	Q. All right.	
	A. And the second sample then,	
5	that second sample was given	
6	Q. Was that then re-assayed on the	ne
7.	RIA method?	
8	A. It was re-assayed. It should	
9	have been given a different sample number but it	
10 m	wasn't.	
11	Q. All right. Was that final	
12	specimen, then, Doctor, as well a specimen of	
,	heart blood?	
13	A. Yes, it was.	
14	Q. Was it run solely on the	
15	RIA or was it run on both techniques?	
16	A. It was run I think solely on	
17 /	the RIA.	
18	Q. All right. Can you tell me	
19	then, Doctor. I assume it was first run neat on the	
	RIA?	
20 '	A. Yes. 098, it was run neat	
21	on 5 times 10 times 20.	
22	Q. All right. And what was the	
23'	result when it was run neat?	
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Commissioner.

- A. It was high, greater than 5.
- Q. All right. And what was it when it was run at a dilution of 5?

A. 24.5, and 24 at times 10 and 22 at times 20.

THE COMMISSIONER'S I'm getting a little alarmed, Miss Cronk.

MS. CRONK: I'm almost finished, Mr.

THE COMMISSIONER: Fine.

 $\qquad \qquad \text{MS. CRONK: Q. With your indulgence,} \\ \text{sir, I will be one moment.}$

THE COMMISSIONER: All right.

MS. CRONK: Q. Doctor, are you saying that the results on this specimen were identical on dilution to the results on Specimen No. 212425 which we spoke about a few moments ago, which was a sample also of heart blood but taken at a different time. The results that you have just read to me are identical, the results that you gave me for Sample No. ---

A. That's right. 212098 was converted in the next reporting and I think you've got a report that is incorrect here. But the next report had that correction made to it. So, you see, there



were two samples, as you yourself pointed out, that are of the same sample number; one that was drawn at 6:45 and one that was drawn at 9.



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Soldin, re-dr.ex. ANGUS, STONEHOUSE & CO. LTD. TORONTO, ONTARIO (Cronk)

But you are saying, Doctor, that 0. the results of the assays --

This is the same sample.

I am sorry, Doctor, it is the same as which sample?

On page 147 of the medical record there are three different samples set out. Do you see that, Doctor?

> Α. Yes.

The third one, Sample No. 212098 Q. you have told me was one specimen, and that there is another specimen which accidentally bore the same specimen number so that there were four in total. And you have just given me the same results?

That is my recollection, yes.

On 212098, the heart blood specimen as you did for the Heart Blood Specimen No. 212425, and my question was merely to confirm that the results were in fact identical?

I don't have the book here with me so that I might be - it might be easier if I just

Perhaps, Doctor, you can let us know subsequently through your counsel if there is any differential on the last specimen numbers that we have just looked at.

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But in any event I take it that the final result of 24 was expressed in namomoles, and it similarly converts to 18.7 nanograms?

A. Yes.

 $\label{eq:MS.CRONK: Thank you, Doctor. I} % \begin{center} \end{center} % \begin{center} \begi$

Thank you, sir.

THE COMMISSIONER: You have no witness available for this afternoon?

MS. CRONK: No, sir, there is not.

Mr. Cimbura will be here at ten tomorrow morning.

THE COMMISSIONER: Thank you, Doctor.

Then we will adjourn until tomorrow

morning.

--- Whereupon the Hearing adjourned at 1:25 p.m. until Wednesday, October 19th, 1983, at 10:00 a.m.



